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#### (54) Title: SECRETED HUMAN PROTEINS

#### (57) Abstract

Secreted proteins can be identified using a method which exploits the ability of microsomes to modify proteins post-translationally. Nineteen human secreted proteins and full-length cDNA sequences encoding the proteins have been identified using this method. The proteins and cDNA sequences can be used, *inter alia*, for targeting other proteins to the membrane or extracellular milieu.

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## SECRETED HUMAN PROTEINS

This application claims the benefit of copending provisional application Serial No. 60/032,757, filed December 11, 1996, which is incorporated herein by reference.

#### TECHNICAL AREA OF THE INVENTION

The invention relates to the area of proteins. More particularly, the invention relates to human secreted proteins.

#### **BACKGROUND OF THE INVENTION**

Secreted proteins include such important proteins as growth factors, cytokines and their receptors, extracellular matrix proteins, and proteases.

Nucleotide sequences encoding these proteins can be used to detect disease states in which such proteins are implicated and to develop therapeutics for such diseases.

Thus, there is a need in the art for methods of identifying secreted proteins and the nucleotide sequences which encode them.

## SUMMARY OF THE INVENTION

It is an object of the invention to provide an isolated and purified human protein.

It is yet another object of the invention to provide a fusion protein.

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It is still another object of the invention to provide a preparation of antibodies.

It is even another object of the invention to provide an isolated and purified subgenomic polynucleotide.

It is yet another object of the invention to provide an isolated gene.

It is a further object of the invention to provide a DNA construct for expressing all or a portion of a human protein.

It is still another object of the invention to provide a host cell comprising a DNA construct.

It is another object of the invention to provide a homologously recombinant cell.

It is even another object of the invention to provide a method of producing a human protein.

It is another object of the invention to provide a method of identifying a secreted polypeptide which is modified by rough microsomes.

These and other objects of the invention are provided by one or more of the embodiments described below.

One embodiment of the invention provides an isolated and purified human protein. The isolated and purified human protein has an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Another embodiment of the invention provides an isolated and purified human protein having an amino acid sequence which is at least 85% identical to an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Still another embodiment of the invention provides a polypeptide comprising at least 6 contiguous amino acids of an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

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Even another embodiment of the invention provides a fusion protein. The fusion protein comprises a first protein segment and a second protein segment fused together by means of a peptide bond. The first protein segment consists of at least 6 contiguous amino acids selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Yet another embodiment of the invention provides a preparation of antibodies. The antibodies specifically bind to a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Even another embodiment of the invention provides an isolated and purified subgenomic polynucleotide. The isolated and purified subgenomic polynucleotide has a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Yet another embodiment of the invention provides an isolated and purified subgenomic polynucleotide consisting of at least 10 contiguous nucleotides selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Still another embodiment of the invention provides an isolated gene. The isolated gene corresponds to a cDNA sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Another embodiment of the invention provides a DNA construct for expressing all or a portion of a human protein. The DNA construct comprises a promoter and a polynucleotide segment. The polynucleotide segment encodes at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

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The polynucleotide segment is located downstream from the promoter.

Transcription of the polynucleotide segment initiates at the promoter.

Even another embodiment of the invention provides a host cell comprising a DNA construct. The DNA construct comprises a promoter and a polynucleotide segment. The polynucleotide segment encodes at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter.

Still another embodiment of the invention provides a homologously recombinant cell having incorporated therein a new transcription initiation unit. The transcription initiation unit comprises in 5' to 3' order an exogenous regulatory sequence, an exogenous exon, and a splice donor site. The transcription initiation unit is located upstream to a coding sequence of a gene. The gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The exogenous regulatory sequence controls transcription of the coding sequence of the gene.

Yet another embodiment of the invention provides a method of producing a human protein. A culture of a cell is grown. The cell comprises a DNA construct. The DNA construct comprises a promoter and a polynucleotide segment. The polynucleotide segment encodes at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter. The protein is purified from the culture.

Even another embodiment of the invention provides a method of producing a human protein. A culture of a cell is grown. The cell comprises a new transcription initiation unit. The transcription initiation unit comprises in 5' to 3'

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order an exogenous regulatory sequence, an exogenous exon, and a splice donor site. The transcription initiation unit is located upstream to a coding sequence of a gene. The gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The exogenous regulatory sequence controls transcription of the coding sequence of the gene. The protein is purified from the culture.

Another embodiment of the invention provides a method of identifying a secreted polypeptide which is modified by rough microsomes. A population of cDNA molecules is transcribed *in vitro* whereby a population of cRNA molecules is formed. A first portion of the population of cRNA molecules is translated *in vitro* in the absence of rough microsomes whereby a first population of polypeptides is formed. A second portion of the population of cRNA molecules is translated *in vitro* in the presence of rough microsomes whereby a second population of polypeptides is formed. The first population of polypeptides is compared with the second population of polypeptides. Polypeptide members of the second population which have been modified by the rough microsomes are detected.

The present invention thus provides the art with a method for identifying secreted proteins or polypeptides, the amino acid sequences of nineteen novel human secreted proteins, and the nucleotide sequences which encode these proteins. The invention can be used to, *inter alia*, to produce secreted proteins for therapeutic and diagnostic purposes.

## **DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS**

The inventors have discovered a method for identifying secreted proteins or polypeptides. Secreted proteins or polypeptides include soluble proteins which can be transported across a membrane, such as a cell membrane, nuclear membrane, or membrane of the endoplasmic reticulum, as well as proteins which can be partially secreted from a cell, such as membrane-bound receptors.

Secreted proteins can contain a signal (or secretion leader) sequence, located at the N-terminus and including at least several hydrophobic amino acids,

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such as phenylalanine, methionine, leucine, valine, or tryptophan. Non-hydrophobic amino acids can also be included in the signal sequence. Signal sequences are described in von Heijne, *J. Mol. Biol. 184*:99-105 (1985) and Kaiser and Botstein, *Mol. Cell. Biol.* 6:2382-2391 (1986). Secreted proteins can also be glycosylated by post-translational modification. The presence of a signal sequence or the presence of glycosylation or both indicate that a particular protein is a secreted protein.

In order to identify secreted proteins or polypeptides, the method of the invention exploits properties of microsomes, which are the closed vesicles that result from fragmentation of endoplasmic reticulum. Microsomes can be rough or smooth, depending on whether the endoplasmic reticulum from which they were derived is studded with ribosomes. Microsomes, particularly rough microsomes, have the ability to perform post-translational modifications, such as glycosylation and cleavage of signal sequences from proteins or polypeptides.

To identify secreted proteins, a population of complementary DNA (cDNA) molecules is transcribed *in vitro* to synthesize a population of complementary RNA (cRNA) molecules. The cDNA molecules can be synthesized by reverse transcription of mRNA molecules isolated from a particular cell or tissue type or organism using, for example, a commercially available reverse transcriptase enzyme. Alternatively, the reverse transcription reaction to form cDNA molecules can be conducted on total RNA, without a preliminary purification of mRNA.

Any organism, such as a bacterium, plant, invertebrate, or vertebrate organism, can be used as a source of RNA. Particularly preferred sources of RNA are mammals, most preferably humans. Tissues, such as liver, brain, kidney, spleen, pancreas, or muscle, can be used as a source of RNA. Individual cell types, either primary cells or members of established cell lines, such as HeLa, CHO, PC12, P19, BHK, COS, or HepG2, are suitable sources of RNA. Tissues or primary cells isolated from organisms at a particular stage in development can be used as RNA sources. Stem cells, such as hematopoietic, neuronal, and embryonic stem cells, can also be used as a source of RNA.

Total RNA or mRNA can be isolated using methods known in the art. Such methods are described, inter alia, in Sambrook et al., MOLECULAR CLONING, A

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LABORATORY MANUAL (2d ed., Cold Spring Harbor Press, N.Y., 1989), and Ausubel et al., CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Greene Publishing Associates and John Wiley & Sons, N.Y., 1994). Techniques for RNA isolation can be tailored for a particular organism or cell type, as is known in the art.

Complementary DNA can optionally be obtained from a cDNA library. The cDNA library can be derived from the genome of any organism of interest, particularly a mammal or a human. Tissue- or cell type-specific cDNA libraries can also be used as a source of cDNA.

Transcription of cDNA molecules in vitro to form cRNA molecules can be carried out using any methods known in the art. These methods include, for example, placing cDNA into a cloning vector containing a promoter, such as an SP6, T7, or T3 polymerase promoter, and transcribing the cDNA using the appropriate polymerase. A variety of commercial kits are available for this purpose.

A first portion of the population of cRNA molecules can be translated in vitro, in the absence of rough microsomes, to form a first population of polypeptides which have not been post-translationally modified. A second portion of the population of cRNA molecules can be translated in vitro in the presence of rough microsomes. Under the conditions of the in vitro translation reaction, rough microsomes can cleave signal sequences from those polypeptides which comprise such sequences. Under the same conditions, rough microsomes can also glycosylate those polypeptides which contain glycosylation sites.

Methods of *in vitro* translation are those which are known in the art, such as translation in a reticulocyte lysate system, particularly a rabbit reticulocyte lysate. Reticulocyte lysate systems can be assembled in the laboratory or purchased commercially in kit form.

Microsomes can be prepared by disruption of tissues or cells by homogenization, as is known in the art. If desired, rough and smooth microsomes can be separated using well-known techniques, such as sucrose density gradient sedimentation. Microsomes are also available commercially, for example, such as the canine pancreatic microsomes available from Promega Corp., Madison, WI.

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The first population of polypeptides can then be compared with the second population of polypeptides. This comparison can be by means of, for example, one-or two-dimensional polyacrylamide gel electrophoresis, as is known in the art. Polypeptides separated in the gels can be detected by any means known in the art, such as staining with copper, silver, Coomassie Brilliant Blue, amido black, fast green FCF, Ponceau S, or a chromophoric label. Separated proteins can also be visualized using radioactive, chemiluminescent, fluorescent, or enzymatic tags incorporated into the proteins before separation.

The gels can be dried or the proteins can be transferred to membranes, such as polyvinylidene difluoride membranes. Either the gels or membranes themselves or photographs of the gels or membranes can be compared by eye. Alternatively, the gels or membranes can be scanned, for example, with a densitometer and analyzed with the aid of a computer.

Polypeptide members of the second population of polypeptides, which have been modified by the rough microsomes, can be detected by any means available in the art. For example, a shift in the position of a polypeptide band can be observed, indicating an increase in molecular weight of a member of the second population compared with the corresponding polypeptide member of the first population. Such an increase in molecular weight indicates that the polypeptide member of the second population was glycosylated by the rough microsomes.

A shift in the position of a polypeptide band indicating a decrease in molecular weight of a member of the second population compared with the corresponding polypeptide member of the first population can also be observed. This decrease in molecular weight indicates that the polypeptide member of the second population contained a signal sequence which was cleaved by the rough microsomes.

Polypeptides which are modified by the rough microsomes are identified as secreted polypeptides. Optionally, quantities of cDNA molecules which encode secreted polypeptides can be obtained. Molecules of cDNA which encode polypeptides which are post-translationally modified by the rough microsomes can be placed into suitable vectors using standard recombinant DNA techniques and

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used to transform host cells. Many vectors are available for this purpose, such as retroviral or adenoviral vectors and bacteriophage, as described below.

Vectors comprising cDNA which encode secreted polypeptides can be introduced into host cells using techniques available in the art. These techniques include, but are not limited to, transferrin-polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, and calcium phosphate-mediated transfection.

The host cells can be any host cells which are capable of propagating cDNA molecules. A variety of host cells, for example immortalized cell lines such as HeLa, CHO, or HEK, are available for this purpose.

Transformed host cells can be diluted serially and cultured to form individual colonies. Methods of culturing host cells and the media suitable for each host cell type are well known in the art. Preferably, each colony originates from a single transformed host cell. Separate preparations of cDNA from each colony can be prepared, as described above, and transcribed *in vitro* to form cRNA. The cRNA can be transcribed to form secreted polypeptides, which can be purified as is known in the art. If the preparation of secreted polypeptides from a colony contains more than one species of polypeptide, the steps described above can be repeated until a colony is obtained which contains cDNA encoding only a single species of polypeptide.

Complementary DNA molecules which encode secreted proteins can be sequenced using standard nucleotide sequencing techniques. The sequence of each cDNA molecule can be compared with known sequences in a database to determine whether the clone encodes a known or a novel secreted protein.

The inventors have used the method of the invention to identify nineteen novel human secreted proteins. Amino acid sequences for these nineteen human secreted proteins are disclosed in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. Nucleotide sequences which encode the proteins are disclosed in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19, respectively.

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Clones containing the cDNAs of the secreted proteins were deposited on December 11, 1997, with the ATCC. Individual bacterial cells (*E. coli*) in this composite deposit contain one or more of the polynucleotides encoding the secreted proteins of the invention and can be retrieved using an oligonucleotide probe designed from the sequence for that particular polynucleotide, as provided herein. Each polynucleotide can be removed from the vector by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI). The deposit submitted to the ATCC has been designated SECP120997. The nucleotide sequences of these deposits and the amino acid sequences they encode are controlling in the event of a discrepancy between the amino acid and nucleotide sequences disclosed herein and those contained in the deposits.

A purified and isolated subgenomic polynucleotide of the present invention comprises at least 10, 12, 15, 18, 20, 25, 30, 35, 40, 45, or 50 contiguous nucleotides selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The isolated and purified subgenomic polynucleotides can comprise an entire nucleotide sequence selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Subgenomic polynucleotides contain less than a whole chromosome and are preferably intron-free. Polynucleotides of the invention can be isolated and purified free from other nucleotide sequences by standard nucleic acid purification techniques, using restriction enzymes and probes to isolate fragments comprising the coding sequences.

Isolated genes corresponding to the cDNA sequences disclosed herein are also provided. Known methods can be used to isolate the corresponding genes using the provided cDNA sequences. These methods include preparation of probes or primers from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 for use in identifying or amplifying the genes from human genomic libraries or other sources of human genomic DNA.

The coding sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 can be made using reverse transcriptase with

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human mRNA as a template. Amplification by PCR can also be used to obtain the polynucleotides, using either genomic DNA or cDNA as a template. Polynucleotide molecules of the invention can also be made using the techniques of synthetic chemistry given the sequences disclosed herein. The degeneracy of the genetic code permits alternate nucleotide sequences which will encode the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 to be synthesized. All such nucleotide sequences are within the scope of the present invention.

Polynucleotide molecules of the invention can be propagated in vectors and cell lines as is known in the art. Polynucleotide molecules can be on linear or circular molecules. They can be on autonomously replicating molecules or on molecules without replication sequences. For propagation, polynucleotides of the invention can be introduced into suitable host cells using any techniques available in the art, as described above.

Subgenomic polynucleotides of the invention can be used to propagate additional copies of the polynucleotides or to express protein, polypeptides, or fusion proteins. The subgenomic polynucleotides disclosed herein can also be used, for example, as biomarkers for tissues or chromosomes, as molecular weight markers for DNA gels, to elicit immune responses, such as the formation of antibodies against single- or double-stranded DNA, and in DNA-ligand interaction assays, to detect proteins or other molecules which interact with the nucleotide sequences.

Disease states may be associated with alterations in the expression of genes which encode proteins of the invention. Polynucleotide sequences disclosed herein can also be used to determine the involvement of any of these sequences in disease states. For example, a gene in a diseased cell can be sequenced and compared with a wild-type coding sequence of the invention. Alternatively, nucleotide probes can be constructed and used to detect normal or altered (mutant) forms of mRNA in a diseased cell. Subgenomic polynucleotides of the invention can also be used to design diagnostic tests and therapeutic compositions for diseases which may be associated with altered expression of these genes.

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The present invention provides both full-length and mature forms of the disclosed proteins. Full-length forms of the proteins have the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The full-length forms of a protein can be processed enzymatically to remove a signal sequence, resulting in a mature form of the protein. Signal sequences can be identified by examination of the amino acid sequences disclosed herein and comparison with amino acid sequences of known signal sequences (see, e.g., von Heijne, 1985; Kaiser & Botstein, 1986). Similarly, transmembrane domains can be identified by examination of the amino acid sequences disclosed herein. A transmembrane domain typically contains a long stretch of 15-30 hydrophobic amino acids.

Other domains with predicted functions can also be identified. For example, the protein having the amino acid sequence shown in SEQ ID NO:23 comprises a Kunitz type serine protease inhibitor domain spanning amino acids 68 to 122 of SEQ ID NO:23. The protein having the amino acid sequence shown in SEQ ID NO:20 contains a zinc-finger motif.

Allelic variants of the disclosed subgenomic polynucleotides can occur and encode proteins which are identical, homologous, or substantially related to amino acid sequences disclosed herein (see below).

Allelic variants of subgenomic polynucleotides of the invention can be identified by hybridization of putative allelic variants with nucleotide sequences disclosed herein under stringent conditions. For example, by using the following wash conditions--2 x SCC, 0.1% SDS, room temperature twice, 30 minutes each; then 2 x SCC, 0.1% SDS, 50 °C. once, 30 minutes; then 2 x SCC, room temperature twice, 10 minutes each--allelic variants can be identified which contain at most about 25-30% basepair mismatches. More preferably, allelic variants contain 15-25% basepair mismatches, even more preferably 5-15% basepair mismatches.

Protein variants of secreted proteins of the invention are also included.

Amino acids which are not involved in regions which determine biological activity can be deleted or modified without affecting biological function. Preferably, protein

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variants of the invention have amino acid sequences which are at least 85%, 90%, or 95% identical to the amino acid sequences disclosed herein and have similar biological properties (see below). More preferably, the molecules are 98% identical. Modifications of interest in the protein sequences can include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue. Proteins or derivatives can be either glycosylated or unglycosylated. Techniques for making such modifications are well known to those skilled in the art (see, e.g., U.S. 4,518,584). Alternatively, variants of proteins disclosed herein can be constructed using techniques of synthetic chemistry or using recombinant DNA methods.

Preferably, amino acid changes in variants or derivatives of proteins of the invention are conservative amino acid changes, i.e., substitutions of similarly charged or uncharged amino acids. A conservative amino acid change involves substitution of one amino acid for another amino acid of a family of amino acids which are structurally related in their side chains. Naturally occurring amino acids are generally divided into four families: acidic (aspartate, glutamate), basic (lysine, arginine, histidine), non-polar (alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), and uncharged polar (glycine, asparagine, glutamine, cystine, serine, threonine, tyrosine) amino acids. Phenylalanine, tryptophan, and tyrosine are sometimes classified as aromatic amino acids. It is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid will not have a major effect on the binding properties of the resulting molecule, especially if the replacement does not involve an amino acid at a binding site involved in an interaction of the protein. Non-naturally occurring amino acids can also be used to form protein variants of the invention.

Whether an amino acid change results in a functional protein or polypeptide can readily be determined by assaying biological properties of the disclosed proteins or polypeptides, as described below. Species homologs of human subgenomic polynucleotides and proteins of the invention can also be identified by making

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suitable probes or primers and screening cDNA expression libraries from other species, such as mice, monkeys, yeast, or bacteria.

In the case of proteins which are membrane-bound, such as cell surface receptor proteins, soluble forms of the proteins can be obtained by deleting the nucleotide sequences which encode part or all of the intracellular and transmembrane domains of the protein and expressing a fully secreted form of the protein in a host cell. Techniques for identifying intracellular and transmembrane domains, such as homology searches, can be used to identify such domains in proteins of the invention using amino acid and nucleotide sequences disclosed herein.

Polypeptides consisting of less than full-length proteins of the present invention are also provided. Polypeptides of the invention can be linear or can be cyclized, for example, as described in Saragovi et al., 1992, Bio/Technology 10, 773-778 and McDowell et al., 1992, J. Amer. Chem. Soc. 114, 9245-9253. Polypeptides can be used, for example, as immunogens, diagnostic aids, or therapeutics, and to create fusion proteins, as described below.

Polypeptide molecules consisting of less than the entire amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 are also provided. Such polypeptides comprise at least 6, 8, 10, 12, 15, 18, or 20 contiguous amino acids of an amino acid sequence shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. Polypeptide molecules of the invention can also possess minor amino acid alterations which do not substantially affect the ability of the polypeptides to interact with specific molecules, such as antibodies.

Derivatives of the polypeptides, such as glycosylated forms, aggregative conjugates with other molecules, and covalent conjugates with unrelated chemical moieties, are also provided. Derivatives also include allelic variants, species variants, and muteins. Covalent derivatives are prepared by linkage of functionalities to groups which are found in the amino acid chain or at the N- or C-terminal residue by means known in the art. Truncations or deletions of regions which do not affect biological function are also encompassed. Truncated or deleted

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polypeptides can be prepared synthetically or recombinantly, or by proteolytic digestion of purified or partially purified secreted proteins of the invention.

Fusion proteins comprising at least 6, 8, 10, 12, 15, 18, or 20 contiguous amino acids of the disclosed proteins can also be constructed. Human fusion proteins are useful, *inter alia*, for generating antibodies against amino acid sequences and for use in various assay systems. For example, fusion proteins can be used to identify proteins which interact with secreted proteins of the invention and influence their function. Physical methods, such as protein affinity chromatography, or library-based assays for protein-protein interactions, such as the yeast two-hybrid or phage display systems, can be used for this purpose. Such methods are well known in the art and can also be used as drug screens. Fusion proteins can also be used to target molecules to a specific location in a cell or to cause a molecule to be secreted or to be anchored in a cellular membrane.

Fusion proteins of the invention comprise two protein segments which are fused together with a peptide bond. The first protein segment comprises at least 6, 8, 10, 12, 15, 18, or 20 contiguous amino acids selected from an amino acid sequence shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The first protein segment can also be a full-length protein (comprising a signal sequence) or a mature protein (lacking a signal sequence). The second protein segment can be a full-length protein or a protein fragment. The second protein or protein fragment can be labeled with a detectable marker, such as a radioactive, chemiluminescent, biotinylated, or fluorescent tag, or can be an enzyme which will generate a detectable product. Enzymes suitable for this purpose, such as β-galactosidase, are well known in the art.

Techniques for making fusion proteins, either recombinantly or by covalently linking two protein segments, are well known in the art. Fusion proteins comprising amino acid sequences of the invention can also be constructed, for example, using standard recombinant DNA methods to make a DNA construct which comprises contiguous nucleotides selected from SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and encoding the desired amino

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acids in proper reading frame with nucleotides encoding the second protein segment.

Proteins or polypeptides of the invention can be purified free from other components with which they are normally associated in a cell, such as carbohydrates, lipids, subcellular organelles, or other proteins. An isolated protein or polypeptide is at least 90% pure. Preferably, the preparations are 95% or 99% pure. The purity of a preparation can be assessed, for example, by examining electrophoretograms of protein or polypeptide preparations at several pH values and at several polyacrylamide concentrations, as is known in the art.

Standard biochemical methods can be used to isolate proteins of the invention from tissues which express the proteins or to isolate proteins, polypeptides, or fusion proteins from recombinant host cells into which a DNA construct has been introduced. Methods of protein purification, such as size exclusion chromatography, ammonium sulfate fractionation, ion exchange chromatography, affinity chromatography, crystallization, electrofocusing, or preparative gel electrophoresis, are well known and widely used in the art.

Alternatively, proteins, fusion proteins, or polypeptides of the invention can be produced by recombinant DNA methods or by synthetic chemical methods. Synthetic chemistry methods, such as solid phase peptide synthesis, can be used to synthesize proteins, fusion proteins, or polypeptides. For production of recombinant proteins, fusion proteins, or polypeptides, coding sequences selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 can be expressed in prokaryotic or eukaryotic host cells using expression systems known in the art. These expression systems include bacterial, yeast, insect, and mammalian cells (see below).

The resulting expressed protein can then be purified from the culture medium or from extracts of the cultured cells using purification procedures known in the art. For example, for proteins fully secreted into the culture medium, cell-free medium can be diluted with sodium acetate and contacted with a cation exchange resin, followed by hydrophobic interaction chromatography. Using this method, the desired protein, fusion protein, or polypeptide is typically greater than 95% pure.

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Further purification can be undertaken, using, for example, any of the techniques listed above. Proteins, fusion proteins, or polypeptides can also be tagged with an epitope, such as a "Flag" epitope (Kodak), and purified using an antibody which specifically binds to that epitope.

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It may be necessary to modify a protein produced in yeast or bacteria, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain a functional protein. Such covalent attachments can be made using known chemical or enzymatic methods.

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Proteins or polypeptides of the invention can also be expressed in cultured cells in a form which will facilitate purification. For example, a secreted protein or polypeptide can be expressed as a fusion protein comprising, for example, maltose binding protein, glutathione-S-transferase, or thioredoxin, and purified using a commercially available kit. Kits for expression and purification of such fusion proteins are available from companies such as New England BioLabs, Pharmacia, and Invitrogen.

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The coding sequences disclosed herein can also be used to construct transgenic animals, such as cows, goats, pigs, or sheep. Female transgenic animals can then produce proteins, polypeptides, or fusion proteins of the invention in their milk. Methods for constructing such animals are known and widely used in the art.

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Used to obtain a preparation of antibodies which specifically bind to epitopes comprising amino acid sequences of the invention. Antibodies of the invention can be used, for example, to detect proteins, polypeptides, or fusion proteins of the invention which are secreted into culture medium or to identify tissues or cells which express these molecules. The antibodies can be polyclonal or monoclonal or can be single chain antibodies. Techniques for raising polyclonal and monoclonal antibodies and for constructing single chain antibodies are well known in the art.

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Antibodies of the invention bind specifically to epitopes comprising amino acid sequences of the invention, preferably to epitopes not present on other proteins. Typically a minimum number of contiguous amino acids to encode an epitope is 6, 8, or 10. However, more amino acids can be part of an epitope, for

example, at least 15, 25, or 50, especially to form epitopes which involve non-contiguous residues. Specific binding antibodies do not detect other proteins on Western blots of proteins or in immunocytochemical assays. Specific binding antibodies provide a signal at least ten-fold lower than the signal provided with epitopes which do not comprise amino acid sequences of the invention. Antibodies which bind specifically to secreted proteins of the invention include those that bind to mature or full-length proteins, to polypeptides or degradation products, to fusion proteins, or to protein variants. In a preferred embodiment of the invention, the antibodies immunoprecipitate the desired protein, fusion protein, or polypeptide from solution and react with the protein, fusion protein, or polypeptide on Western blots of polyacrylamide gels.

Techniques for purifying antibodies are those which are available in the art. In a preferred embodiment, antibodies are affinity purified by passing the antibodies over a column to which amino acid sequences of the invention are bound. The bound antibody is then eluted, for example using a buffer with a high salt concentration. Any such technique may be chosen to purify antibodies of the invention.

The invention also provides DNA constructs, for expressing all or a portion of a protein of the invention in a host cell. The DNA construct comprises a promoter which is functional in the particular host cell selected. The skilled artisan can readily select an appropriate promoter from the large number of cell type-specific promoters known and used in the art. The DNA construct can also contain a transcription terminator which is functional in the host cell.

The expression construct comprises a polynucleotide segment which encodes all or a portion of a human protein encoded by SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 or a variant thereof. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter. DNA constructs can be linear or circular and can contain sequences, if desired, for autonomous replication.

The host cell comprising the DNA construct can be any suitable prokaryotic or eukaryotic cell. Expression systems in bacteria include those described in Chang

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et al., Nature (1978) 275: 615; Goeddel et al., Nature (1979) 281: 544; Goeddel et al., Nucleic Acids Res. (1980) 8: 4057; EP 36,776; U.S. 4,551,433; deBoer et al., Proc. Natl. Acad. Sci. USA (1983) 80: 21-25; and Siebenlist et al., Cell (1980) 20: 269.

Expression systems in yeast include those described in Hinnen et al., Proc.

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Natl. Acad. Sci. USA (1978) 75: 1929; Ito et al., J. Bacteriol. (1983) 153: 163; Kurtz et al., Mol. Cell. Biol. (1986) 6: 142; Kunze et al., J. Basic Microbiol. (1985) 25: 141; Gleeson et al., J. Gen. Microbiol. (1986) 132: 3459, Roggenkamp et al., Mol. Gen. Genet. (1986) 202:302); Das et al., J. Bacteriol. (1984) 158: 1165; De Louvencourt et al., J. Bacteriol. (1983) 154: 737, Van den Berg et al., Bio/Technology (1990) 8: 135; Kunze et al., J. Basic Microbiol. (1985) 25: 141; Cregg et al., Mol. Cell. Biol. (1985) 5: 3376; U.S. 4,837,148; U.S. 4,929,555; Beach and Nurse, Nature (1981) 300: 706; Davidow et al., Curr. Genet. (1985) 10: 380; Gaillardin et al., Curr. Genet. (1985) 10: 49; Ballance et al., Biochem. Biophys. Res. Commun. (1983) 112: 284-289; Tilburn et al., Gene (1983) 26: 205-22;, Yelton et al., Proc. Natl. Acad. Sci. USA (1984) 81: 1470-1474; Kelly and Hynes, EMBO J. (1985) 4: 475479; EP 244,234; and WO 91/00357.

Expression of heterologous genes in insects can be accomplished as

described in U.S. 4,745,051; Friesen et al. (1986) "The Regulation of Baculovirus Gene Expression" in: The Molecular Biology of Baculoviruses (W. Doerfler, ed.); EP 127,839; EP 155,476; Vlak et al., J. Gen. Virol. (1988) 69: 765-776; Miller et al., Ann. Rev. Microbiol. (1988) 42: 177; Carbonell et al., Gene (1988) 73: 409; Maeda et al., Nature (1985) 315: 592-594; Lebacq-Verheyden et al., Mol. Cell. Biol. (1988) 8: 3129; Smith et al., Proc. Natl. Acad. Sci. USA (1985) 82: 8404; Miyajima et al., Gene (1987) 58: 273; and Martin et al., DNA (1988) 7:99. Numerous baculoviral strains and variants and corresponding permissive insect host cells from hosts are described in Luckow et al., Bio/Technology (1988) 6: 47-55, Miller et al., in Generic Engineering (Setlow, J.K. et al. eds.), Vol. 8 (Plenum Publishing, 1986), pp. 277-279; and Maeda et al., Nature, (1985) 315: 592-594.

Mammalian expression can be accomplished as described in Dijkema et al.,

EMBO J. (1985) 4: 761; Gorman et al., Proc. Natl. Acad. Sci. USA (1982b) 79: 6777; Boshart et al., Cell (1985) 41: 521; and U.S. 4,399,216. Other features of mammalian expression can be facilitated as described in Ham and Wallace, Meth. Enz. (1979) 58: 44; Barnes and Sato, Anal. Biochem. (1980) 102: 255; U.S. 4,767,704; U.S. 4,657,866; U.S. 4,927,762; U.S. 4,560,655; WO 90/103430, WO 87/00195, and U.S. RE 30,985.

DNA constructs of the invention can be introduced into host cells using any technique known in the art. These techniques include transferrin-polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, and calcium phosphate-mediated transfection.

Alternatively, expression of an endogenous gene encoding a protein of the invention can be manipulated by introducing by homologous recombination a DNA construct comprising a transcription unit in frame with the endogenous gene, to form a homologously recombinant cell comprising the transcription unit. The transcription unit comprises a targeting sequence, a regulatory sequence, an exon, and an unpaired splice donor site. The new transcription unit can be used to turn the endogenous gene on or off as desired. This method of affecting endogenous gene expression is taught in U.S. 5,641,670, which is incorporated herein by reference.

The targeting sequence is a segment of at least 10, 12, 15, 20, or 50 contiguous nucleotides selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The transcription unit is located upstream to a coding sequence of the endogenous gene. The exogenous regulatory sequence directs transcription of the coding sequence of the endogenous gene.

Secreted proteins of the invention have a variety of uses. For example, secreted proteins can be used in assays to determine biological activities, such as cytokine, cell proliferation, or cellular differentiation activities, tissue growth or

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regeneration, activin or inhibin activity, chemotactic or chemokinetic activity, hemostatic or thrombolytic activity, receptor/ligand activity, tumor inhibition, or anti-inflammatory activity. Assays for these activities are known in the art and are disclosed, for example, in U.S. 5,654,173, which is incorporated herein by reference.

Proteins of the invention can also be used as biomarkers, to identify tissues or cell types which express the proteins, or a stage- or disease-specific alteration in protein expression. Proteins of the invention can be used in protein interaction assays, to identify ligands or binding proteins. Compounds which affect the biological activities of the secreted proteins or their ability to interact with specific ligands can be identified using proteins of the invention in screening assays. Proteins and antibodies of the invention can also be used to design diagnostic tests and therapeutic compositions for diseases which may be associated with altered expression of these proteins. Fusion proteins comprising, for example, signal sequences or transmembrane domains of the disclosed proteins, can be used to target other protein domains to cellular locations in which the domains are not normally found, such as bound to a cellular membrane or secreted extracellularly.

Further objects, features, and advantages of the present invention will readily occur to the skilled artisan provided with the disclosure above.

#### SYNOPSIS OF THE INVENTION

- 1. An isolated and purified human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.
- 2. An isolated and purified human protein having an amino acid sequence which is at least 85% identical to an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

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3. The isolated and purified human protein of item 2 wherein the amino acid sequence is at least 90% identical.

- 4. The isolated and purified human protein of item 2 wherein the amino acid sequence is at least 95% identical.
- 5. The isolated and purified human protein of item 2 wherein the amino acid sequence is at least 98% identical.
- 6. An isolated and purified human polypeptide comprising at least 6 contiguous amino acids of an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.
- 7. A fusion protein comprising a first protein segment and a second protein segment fused together by means of a peptide bond, wherein the first protein segment consists of at least 6 contiguous amino acids selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.
- 8. A preparation of antibodies which specifically bind to the human protein of item 1.
- 9. The preparation of antibodies of item 8 wherein the antibodies are monoclonal.
- 10. The preparation of antibodies of item 8 wherein the antibodies are polyclonal.
- 11. The preparation of antibodies of item 8 wherein the antibodies are single chain antibodies.
- 12. An isolated and purified subgenomic polynucleotide having a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.
- 13. An isolated and purified subgenomic polynucleotide consisting of at least 10 contiguous nucleotides of a nucleotide sequence selected from the group

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consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

- 14. An isolated gene corresponding to a cDNA sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.
- 15. A DNA construct for expressing all or a portion of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, comprising:

a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of the human protein, wherein the polynucleotide segment is located downstream from the promoter, wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

16. A host cell comprising a DNA construct comprising:a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the pormoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

- 17. A homologously recombinant cell having incorporated therein a new transcription initiation unit, wherein the new transcription initiation unit comprises in 5' to 3' order:
  - (a) an exogenous regulatory sequence;
  - (b) an exogenous exon; and
  - (c) a splice donor site,

wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group

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consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19, and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene.

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- 18. A method of producing a human protein, comprising the steps of: growing a culture of a cell comprising a DNA construct comprising (1) a promoter and (2) a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the promoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter; and; purifying the protein from the culture.
- 19. A method of producing a human protein, comprising the steps of:
  growing a culture of a homologously recombinant cell having
  incorporated therein a new transcription initiation unit, wherein the new
  transcription initiation unit comprises in 5' to 3' order:
  - (a) an exogenous regulatory sequence;
  - (b) an exogenous exon; and
  - (c) a splice donor site,

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wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene; and purifying the protein from the culture.

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20. A method of identifying a secreted polypeptide which is modified by rough microsomes, comprising the steps of:

transcribing in vitro a population of cDNA molecules whereby a population of cRNA molecules is formed;

translating a first portion of the population of cRNA molecules in vitro in the absence of rough microsomes whereby a first population of polypeptides is formed;

translating a second portion of the population of cRNA molecules in vitro in the presence of rough microsomes whereby a second population of polypeptides is formed;

comparing the first population of polypeptides with the second population of polypeptides; and

detecting polypeptide members of the second population which have been modified by the rough microsomes.

- 21. The method of item 20 wherein the population of cDNA molecules is synthesized by reverse transcription of a population of mRNA molecules.
- 22. The method of item 21 wherein the mRNA molecules are isolated from a mammal.
- 23. The method of item 22 wherein the mRNA molecules are isolated from a human.
- 24. The method of item 20 wherein the population of cDNA molecules is obtained from a cDNA library.
- 25. The method of item 24 wherein the cDNA library is derived from a mammalian genome.
- 26. The method of item 25 wherein the cDNA library is derived from a human genome.

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## SEQUENCE LISTING

- (1) GENERAL INFORMATION
- (i) APPLICANT: Chiron Corporation
- (ii) TITLE OF THE INVENTION: Secreted Human Proteins
- (iii) NUMBER OF SEQUENCES: 38
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE: Banner & Witcoff
  - (B) STREET: 1001 G Street, NW
  - (C) CITY: Washington
  - (D) STATE: DC
  - (E) COUNTRY: USA
  - (F) ZIP: 20001
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE: Diskette
  - (B) COMPUTER: IBM Compatible
  - (C) OPERATING SYSTEM: DOS
  - (D) SOFTWARE: FastSEQ for Windows Version 2.0
- (vi) CURRENT APPLICATION DATA:
  - (A) APPLICATION NUMBER:
  - (B) FILING DATE: 11-DEC-1997

| (C | ) CL? | SSIF | ICAT | ION |
|----|-------|------|------|-----|
|----|-------|------|------|-----|

- (vii) PRIOR APPLICATION DATA:
  - (A) APPLICATION NUMBER: 60/032757
  - (B) FILING DATE: 11-DEC-1996

#### (viii) ATTORNEY/AGENT INFORMATION:

- (A) NAME: Kagan, Sarah A
- (B) REGISTRATION NUMBER: 32141
- (C) REFERENCE/DOCKET NUMBER:

#### 2441.39505;1369.002;1452.001

- (ix) TELECOMMUNICATION INFORMATION:
  - (A) TELEPHONE: 202-508-9100
  - (B) TELEFAX: 202-508-9299
  - (C) TELEX:
  - (2) INFORMATION FOR SEQ ID NO:1:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 2063 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ix) FEATURE:
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

| GAATTCGGCA | CGAGGCCTCA | GTCTTCCAGG | GCGGCGGTGG | GTGTCCGCTT | CTCTCTGCTC | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| TTCGACTGCA | CCGCACTCGC | GCGTGACCCT | GACTCCCCCT | AGTCAGCTCA | GCGGTGCTGC | 120 |
| CATGGCGTGG | CGGCGCGCG  | AAGCCGGCGT | CGGGGCTCGC | GCCGTGTTGG | CTCTGGCGTT | 180 |
| GCTCGCCCTG | GCCCTGTGCG | TGCCCGGGGC | CCGGGGCCGG | GCTCTCGAGT | GGTTCTCGGC | 240 |

| CGTGGTAAAC | ATCGAGTACG | TGGACCCGCA | GACCAACCTG | ACGGTGTGGA | GCGTCTCGGA | 300  |
|------------|------------|------------|------------|------------|------------|------|
| GAGTGGCCGC | TTCGGCGACA | GCTCGCCCAA | GGAGG CGCG | CATGGCCTGG | TGGGCGTCCC | 360  |
| GTGGGCGCCC | GGCGGAGACC | TCGAGGGCTG | CGCGCCCGAC | ACGCGCTTCT | TCGTGCCCGA | 420  |
| GCCCGGCGGC | CGAGGGGCCG | CGCCCTGGGT | CGCCCTGGTG | GCTCGTGGGG | GCTGCACCTT | 480  |
| CAAGGACAAG | GTGCTGGTGG | CGGCGCGAG  | GAACGCCTCG | GCCGTCGTCC | TCTACAATGA | 540  |
| GGAGCGCTAC | GGGAACATCA | CCTTGCCCAT | GTCTCACGCG | GGAACAGGAA | ATATAGTGGT | 600  |
| CATTATGATT | AGCTATCCAA | AAGGAAGAGA | AATTTTGGAG | CTGGTGCAAA | AAGGAATTCC | 660  |
| AGTAACGATG | ACCATAGGGG | TTGGCACCCG | GCATGTACAG | GAGTTCATCA | GCGGTCAGTC | 720  |
| TGTGGTGTTT | GTGGCCATTG | CCTTCATCAC | CATGATGATT | ATCTCGTTAG | CCTGGCTAAT | 780  |
| ATTTTACTAT | ATACAGCGTT | TCCTATATAC | TGGCTCTCAG | ATTGGAAGTC | AGAGCCATAG | 840  |
| AAAAGAAACT | AAGAAAGTTA | TTGGCCAGCT | TCTACTTCAT | ACTGTAAAGC | ATGGAGAAAA | 900  |
| GGGAATTGAT | GTTGATGCTG | AAAATTGTGC | AGTGTGTATT | GAAAATTTCA | AAGTAAAGGA | 960  |
| TATTATTAGA | ATTCTGCCAT | GCAAGCATAT | TTTTCATAGA | ATATGCATTG | ACCCATGGCT | 1020 |
| TTTGGATCAC | CGAACATGTC | CAATGTGTAA | ACTTGATGTC | ATCAAAGCCC | TAGGATATTG | 1080 |
| GGGAGAGCCT | GGGGATGTAC | AGGAGATGCC | TGCTCCAGAA | TCTCCTCCTG | GAAGGGATCC | 1140 |
| AGCTGCAAAT | TTGAGTCTAG | CTTTACCAGA | TGATGACGGA | AGTGATGACA | GCAGTCCACC | 1200 |
| ATCAGCCTCC | CCTGCTGAAT | CTGAGCCACA | GTGTGATCCC | AGCTTTAAAG | GAGATGCAGG | 1260 |
| AGAAAATACG | GCATTGCTAG | AAGCCGGCAG | GAGTGACTCT | CGGCATGGAG | GACCCATCTC | 1320 |
| CTAGCACACG | TGCCCACTGA | AGTGGCACCA | ACAGAAGTTT | GGCTTGAACT | AAAGGACATT | 1380 |
| TTATTTTTT  | TACTTTAGCA | CATAATTTGT | ATATTTGAAA | ATAATGTATA | TTATTTTACC | 1440 |
| TATTAGATTC | TGATTTGATA | TACAAAGGAC | TAAGATATTT | TCTTCTTGAA | GAGACTTTTC | 1500 |
| GATTAGTCCT | CATATATTA  | TCTACTAAAA | TAGAGTGTTT | ACCATGAACA | GTGTGTTGCT | 1560 |
| TCAGACTATT | ACAAAGACAA | CTGGGGCAGG | TACTCTAATA | TAAAGGACAG | GTGGTGTTTC | 1620 |
| TAAATAATTG | GCTGCTATGG | TTCTGTAAAA | ACCAGTTAAT | TCTATTTTTC | AAGGTTTTTG | 1680 |
| GCAAAGCACA | TCAATGTTAG | ACTAGTTGAA | GTGGAATTGT | ATAATTCAAT | TCGATAATTG | 1740 |
| ATCTCATGGG | CTTTCCCTGG | AGGAAAGGTT | TTTTTTGTTG | TTTTTTTTT  | AAGAACTTGA | 1800 |
| AACTTGTAAA | CTGAGATGTC | TGTAGCTTTT | TTGCCCATCT | GTAGTGTATG | TGAAGATTTC | 1860 |
| AAAACCTGAG | AGCACTTTTT | CTTTGTTTAG | AATTATGAGA | AAGGCACTAG | ATGACTTTAG | 1920 |
| GATTTGCATT | TTTCCCTTTA | TTGCCTCATT | TCTTGTGACG | CCTTGTTGGG | GAGGGAAATC | 1980 |
| TGTTTATTTI | TTCCTACAAA | TAAAAAGCTA | AGATTCTATA | TCGCAAAAA  | ААААААААА  | 2040 |
| ААААААААА  | TTCCTGCGGC | CGC        |            |            |            | 2063 |

## (2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1328 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

| GAATTCGGCA | CGAGGTAGGC | AAGGGATAAA | AAGGCACCTA | AGGCCCTTTT | GCAATAAGAA | 60   |
|------------|------------|------------|------------|------------|------------|------|
| GCCAGATGGA | TAAAGGAAGT | GCTGGTCACC | CTGGAGGTGT | ACTGGTTTGG | GGAAGGTCCC | 120  |
| CGGCCCCAC  | AGCCCTCTGG | GGAGCCTCAC | CCTGGCTCTC | CCCACTCACC | TCAGCCCTCA | 180  |
| GGCAGCCCCT | CCACAGGGCC | CCTCTCCTGC | CTGGACAGCT | CTGCTGGTCT | CCCCGTCCCC | 240  |
| TGGAGAAGAA | CAAGGCCATG | GGTCGGCCCC | TGCTGCTGCC | CCTGCTGCTC | CTGCTGCAGC | 300  |
| CGCCAGCATT | TCTGCAGCCT | GGTGGCTCCA | CAGGATCTGG | TCCAAGCTAC | CTTTATGGGG | 360  |
| TCACTCAACC | AAAACACCTC | TCAGCCTCCA | TGGGTGGCTC | TGTGGAAATC | CCCTTCTCCT | 420  |
| TCTATTACCC | CTGGGAGTTA | GCCATAGTTC | CCAACGTGAG | AATATCCTGG | AGACGGGGCC | 480  |
| ACTTCCACGG | GCAGTCCTTC | TACAGCACAA | GGCCGCCTTC | CATTCACAAG | GATTATGTGA | 540  |
| ACCGGCTCTT | TCTGAACTGG | ACAGAGGGTC | AGGAGAGCGG | CTTCCTCAGG | ATCTCAAACC | 600  |
| TGCGGAAGGA | GGACCAGTCT | GTGTATTTCT | GCCGAGTCGA | GCTGGACACC | CGGAGATCAG | 660  |
| GGAGGCAGCA | GTTGCAGTCC | ATCAAGGGGA | CCAAACTCAC | CATCACCCAG | GCTGTCACAA | 720  |
| CCACCACCAC | CTGGAGGCCC | AGCAGCACAA | CCACCATAGC | CGGCCTCAGG | GTCACAGAAA | 780  |
| GCAAAGGGCA | CTCAGAATCA | TGGCACCTAA | GTCTGGACAC | TGCCATCAGG | GTTGCATTGG | 840  |
| CTGTCGCTGT | GCTCAAAACT | GTCATTTTGG | GACTGCTGTG | CCTCCTCCTC | CTGTGGTGGA | 900  |
| GGAGAAGGAA | AGGTAGCAGG | GCGCCAAGCA | GTGACTTCTG | ACCAACAGAG | TGTGGGGAGA | 960  |
| AGGGATGTGT | ATTAGCCCCG | GAGGACGTGA | TGTGAGACCC | GCTTGTGAGT | CCTCCACACT | 1020 |
| CGTTCCCCAT | TGGCAAGATA | CATGGAGAGC | ACCCTGAGGA | CCTTTAAAAG | GCAAAGCCGC | 1080 |
| AAGGCAGAAG | GAGGCTGGGT | CCCTGAATCA | CCGACTGGAG | GAGAGTTACC | TACAAGAGCC | 1140 |
| TTCATCCAGG | AGCATCCACA | CTGCAATGAT | ATAGGAATGA | GGTCTGAACT | CCACTGAATT | 1200 |
| AAACCACTGG | CATTTGGGGG | CTGTTTATTA | TAGCAGTGCA | AAGAGTTCCT | TTATCCTCCC | 1260 |
| CAAGGATGGA | AAAATACAAT | TTATTTTGCT | TACCATAAAA | алааааааа  | AAAAATTCCT | 1320 |
| GCGGCCGC   |            |            |            |            |            | 1328 |

- (2) INFORMATION FOR SEQ ID NO:3:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1689 base pairs
  - (B) TYPE: nucleic acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

| GAATTCGGCA | CGAGGGCAAG | ATTCGATACA | AAACCAATGA | ACCTGTGTGG          | GAGGAAAACT | 60   |
|------------|------------|------------|------------|---------------------|------------|------|
| TCACTTTCTT | CATTCACAAT | CCCAAGCGCC | AGGACCTTGA | AGTTGAGGTC          | AGAGACGAGC | 120  |
| AGCACCAGTG | TTCCCTGGGG | AACCTGAAGG | TCCCCTCAG  | CCAGCTGCTC          | ACCAGTGAGG | 180  |
| ACATGACTGT | GAGCCAGCGC | TTCCAGCTCA | GTAACTCGGG | TCCAAACAGC          | ACCATCAAGA | 240  |
| TGAAGATTGC | CCTGCGGGTG | CTCCATCTCG | AAAAGCGAGA | AAGGCCTCCA          | GACCACCAAC | 300  |
| ACTCAGCTCA | AGTCAAACGT | CCCTCTGTGT | CCAAAGAGGG | GAGGAAAACA          | TCCATCAAAT | 360  |
| CTCATATGTC | TGGGTCTCCA | GGCCCTGGTG | GCAGCAACAC | AGCTCCATCC          | ACACCAGTCA | 420  |
| TTGGGGGCAG | TGATAAGCCT | GGTATGGAAG | AAAAGGCCCA | GCCCCTGAG           | GCCGGCCCTC | 480  |
| AGGGGCTGCA | CGACCTGGGC | AGAAGCTCCT | CCAGCCTCCT | GGCCTCCCCA          | GGCCACATCT | 540  |
| CAGTCAAGGA | GCCGACCCC  | AGCATCGCCT | CGGACATCTC | GCTGCCCATC          | GCCACCCAGG | 600  |
| AGCTGCGGCA | AAGGCTGAGG | CAGCTGGAAA | ACGGGACGAC | CCTGGGACAG          | TCTCCACTGG | 660  |
| GGCAGATCCA | GCTGACCATC | CGGCACAGCT | CGCAGAGAAA | CAAGCTTATC          | GTGGTCGTGC | 720  |
| ATGCCTGCAG | AAACCTCATT | GCCTTCTCTG | AAGACGGCTC | TGACCCCTAT          | GTCCGCATGT | 780  |
| ATTTATTACC | AGACAAGAGG | CGGTCAGGAA | GGAGGAAAAC | ACACGTGTCA          | AAGAAAACAT | 840  |
| TAAATCCAGT | GTTTGATCAA | AGCTTTGATT | TCAGTGTTTC | GTTACCAGAA          | GTGCAGAGGA | 900  |
| GAACGCTCGA | CGTTGCCGTG | AAGAACAGTG | GCGGCTTCCT | GTCCAAAGAC          | AAAGGGCTCC | 960  |
| TTGGCAAAGT | ATTGGTTGCT | CTGGCATCTG | AAGAACTTGC | CAAAGGCTGG          | ACCCAGTGGT | 1020 |
| ATGACCTCAC | GGAAGATGGG | ACGAGGCCTC | AGGCGATGAC | ATAGCCGCAG          | CAGGCAGGAG | 1080 |
| GCGTCCTCTT | CAGCGTAGCT | CTCCACCTCT | ACCCGGAACA | CACCCTCTCA          | CAGACGTACC | 1140 |
| AATGTTATTT | TTATAATTTC | ATGGATTTAG | TTATACATAC | CTTAATAGTT          | TTATAAAATT | 1200 |
| GTTGACATTT | CAGGCAAATT | TGGCCAATAT | TATCATTGAA | TTTTCTGTGT          | TGGATTTCCT | 1260 |
| CTAGGATTTC | GCCAGTTCCT | ACAACGTGCA | GTAGGGCGGC | GGTAGCTCTT          | GTGTCTGTGG | 1320 |
| ACTCTGCTCA | GCTGTGTCCG | TAGGAGTCGG | ATGTGTCTGT | GCTTTATTAT          | GGCCTTGTTT | 1380 |
| ATATATCACT | GAGGTATACT | ATGCCATGTA | AATAGACTAT | TTTTTATAAT          | CTTAACATGC | 1440 |
| TGGTTTAAAT | TCAGAAGGAA | ATAGATCAAG | GAAATATATA | TATTTTCTTC          | TAAAACTTAT | 1500 |
| TAAATTCGTG | TGACAAATAA | TCATTTTCAT | CTTGGCAGCA | AAAAGTTCTC          | AGTGACCTAT | 1560 |
| TTTGTGGTGT | TTCTTTTTGA | AAAGAAAAGC | TGAAATATTA | TT <u>A</u> AATGCTA | GTATGTTTCT | 1620 |
| GCCCATTATG | AAAGATGAAA | TAAAGTATTC | AAAATATTAA | АААААААА            | AAAAAATTCC | 1680 |
| TGCGGCCGC  |            |            |            |                     |            | 1689 |

## (2) INFORMATION FOR SEQ ID NO:4:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1505 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

| GAATTCGGCA | CGAGGAGCAG | ATCTGCAAGA | GTTTCGTTTA | TGGAGGCTGC | TTGGGCAACA | 60   |
|------------|------------|------------|------------|------------|------------|------|
| AGAACAACTA | CCTTCGGGAA | GAAGAGTGCA | TTCTAGCCTG | TCGGGGTGTG | CAAGGTGGGC | 120  |
| CTTTGAGAGG | CAGCTCTGGG | GCTCAGGCGA | CTTTCCCCCA | GGGCCCTCC  | ATGGAAAGGC | 180  |
| GCCATCCAGT | GTGCTCTGGC | ACCTGTCAGC | CCACCCAGTT | CCGCTGCAGC | AATGGCTGCT | 240  |
| GCATCGACAG | TTTCCTGGAG | TGTGACGACA | CCCCCAACTG | CCCGACGCC  | TCCGACGAGG | 300  |
| CTGCCTGTGA | AAAATACACG | AGTGGCTTTG | ACGAGCTCCA | GCGCATCCAT | TTCCCCAGCG | 360  |
| ACAAAGGGCA | CTGCGTGGAC | CTGCCAGACA | CAGGACTCTG | CAAGGAGAGC | ATCCCGCGCT | 420  |
| GGTACTACAA | CCCCTTCAGC | GAACACTGCG | CCCGCTTTAC | CTATGGTGGT | TGTTACGGCA | 480  |
| ACAAGAACAA | CTTTGAGGAA | GAGCAGCAGT | GCCTCGAGTC | TTGTCGCGGC | ATCTCCAAGA | 540  |
| AGGATGTGTT | TGGCCTGAGG | CGGGAAATCC | CCATTCCCAG | CACAGGCTCT | GTGGAGATGG | 600  |
| CTGTCGCAGT | GTTCCTGGTC | ATCTGCATTG | TGGTGGTGGT | AGCCATCTTG | GGTTACTGCT | 660  |
| TCTTCAAGAA | CCAGAGAAAG | GACTTCCACG | GACACCACCA | CCACCCACCA | CCCACCCCTG | 720. |
| CCAGCTCCAC | TGTCTCCACT | ACCGAGGACA | CGGAGCACCT | GGTCTATAAC | CACACCACGC | 780  |
| GCCCCTCTG  | AGCCTGGGTC | TCACCGGCTC | TCACCTGGCC | CTGCTTCCTG | CTTGCCAAGG | 840  |
| CAGAGGCCTG | GGCTGGGAAA | AACTTTGGAA | CCAGACTCTT | GCCTGTTTCC | CAGGCCCACT | 900  |
| GTGCCTCAGA | GACCAGGGCT | CCAGCCCCTC | TTGGAGAAGT | CTCAGCTAAG | CTCACGTCCT | 960  |
| GAGAAAGCTC | AAAGGTTTGG | AAGGAGCAGA | AAACCCTTGG | GCCAGAAGTA | CCAGACTAGA | 1020 |
| TGGACCTGCC | TGCATAGGAG | TTTGGAGGAA | GTTGGAGTTT | TGTTTCCTCT | GTTCAAAGCT | 1080 |
| GCCTGTCCCT | ACCCCATGGT | GCTAGGAAGA | GGAGTGGGGT | GGTGTCAGAC | CCTGGAGGCC | 1140 |
| CCAACCCTGT | CCTCCCGAGC | TCCTCTTCCA | TGCTGTGCGC | CCAGGGCTGG | GAGGAAGGAC | 1200 |
| TTCCCTGTGT | AGTTTGTGCT | GTAAAGAGTT | GCTTTTTGTT | TATTTAATGC | TGTGGCATGG | 1260 |
| GTGAAGAGGA | GGGGAAGAGG | CCTGTTTGGC | CTCTCTATCC | TCTCTTCCTC | TTCCCCCAAG | 1320 |
| ATTGAGCTCT | CTGCCCTTGA | TCAGCCCCAC | CCTGGCCTAG | ACCAGCAGAC | AGAGCCAGGA | 1380 |
| GAAGCTCAGC | TGCATTCCGC | AGCCCCCACC | CCCAAGGTTC | TCCAACATCA | CAGCCCAGCC | 1440 |
| CGCCCACTGG | GTAATAAAAG | TGGTTTGTGG | ААААААААА  | ААААААААА  | AAGTCCTGCG | 1500 |

GCCGC 1505

## (2) INFORMATION FOR SEQ ID NO:5:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2002 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

| GAATTCGGCA | CGAGGGCCAT | GGCCGGGCTA | TCCCGCGGGT | CCGCGCGCGC | ACTGCTCGCC | 60   |
|------------|------------|------------|------------|------------|------------|------|
| GCCCTGCTGG | CGTCGACGCT | GTTGGCGCTG | CTCGTGTCGC | CCGCGCGGG  | TCGCGGCGGC | 120  |
| CGGGACCACG | GGGACTGGGA | CGAGGCCTCC | CGGCTGCCGC | CGCTACCACC | CCGCGAGGAC | 180  |
| GCGGCGCGCG | TGGCCCGCTT | CGTGACGCAC | GTCTCCGACT | GGGGCGCTCT | GGCCACCATC | 240  |
| TCCACGCTGG | AGGCGGTGCG | CGGCCGGCCC | TTCGCCGACG | TCCTCTCGCT | CAGCGACGGG | 300  |
| CCCCGGGCG  | CGGGCAGCGG | CGTGCCCTAT | TTCTACCTGA | GCCCGCTGCA | GCTCTCCGTG | 360  |
| AGCAACCTGC | AGGAGAATCC | ATATGCTACA | CTGACCATGA | CTTTGGCACA | GACCAACTTC | 420  |
| TGCAAGAAAC | ATGGATTTGA | TCCACAAAGT | CCCCTTTGTG | TTCACATAAT | GCTGTCAGGA | 480  |
| ACTGTGACCA | AGGTGAATGA | AACAGAAATG | GATATTGCAA | AGCATTCGTT | ATTCATTCGA | 540  |
| CACCCTGAGA | TGAAAACCTG | GCCTTCCAGC | CATAATTGGT | TCTTTGCTAA | GTTGAATATA | 600  |
| ACCAATATCT | GGGTCCTGGA | CTACTTTGGT | GGACCAAAAA | TCGTGACACC | AGAAGAATAT | 660  |
| TATAATGTCA | CAGTTCAGTG | AAGCAGACTG | TGGTGAATTT | AGCAACACTT | ATGAAGTTTC | 720  |
| TTAAAGTGGC | TCATACACAC | TTAAAAGGCT | TAATGTTTCT | CTGGAAAGCG | TCCCAGAATA | 780  |
| TTAGCCAGTT | TTCTGTCACA | TGCTGGTTTG | TTTGCTTGCT | TGTTTACTTG | CTTGTTTACC | 840  |
| AATAGAGTTG | ACCTGTTATT | GGATTTCCTG | GAAGATGTGG | TAGCTACTTT | TTTCCTATTT | 900  |
| TGAAGCCATT | TTCGTAGAGA | AATATCCTTC | ACTATAATCA | AATAAGTTTT | GTCCCATCAA | 960  |
| TTCCAAAGAT | GTTTCCAGTG | GTGCTCTTGA | AGAGGAATGA | GTACCAGTTT | TAAATTGCCC | 1020 |
| ATTGGCATTT | GAAGGTAGTT | GAGTATGTGT | TCTTTATTCC | TAGAAGCCAC | TGTGCTTGGT | 1080 |
| AGAGTGCATC | ACTCACCACA | GCTGCCTCTT | GAGCTGCCTG | AGCCTGGTGC | AAAAGGATTG | 1140 |
| GCCCCATTA  | TGGTGCTTCT | GAATAAATCT | TGCCAAGATA | GACAAACAAT | GATGAAACTC | 1200 |
| AGATGGAGCT | TCCTACTCAT | GTTGATTTAT | GTCTCACAAT | CCTGGGTATT | GTTAATTCAA | 1260 |
| CATAGGGTGA | AACTATTTCT | GATAAAGAAC | TTTTGAAAAA | CTTTTTATAC | TCTAAAGTGA | 1320 |
| TACTCAGAAC | AAAAGAAAGT | CATAAAACTC | CTGAATTTAA | TTTCCCCACC | TAAGTCGAGA | 1380 |

| CAGTATTATC | AAAACACATG | TGCACACAGA | TTATTTTTTG | GCTCCAAAAC | TGGATTGCAA | 1440 |
|------------|------------|------------|------------|------------|------------|------|
| AAGAAAGAGG | AGAGATATTT | TGTGTGTTCC | TGGTATTCTT | TTATAAGTAA | AGTTACCCAG | 1500 |
| GCATGGACCA | GCTTCAGCCA | GGGACAAAAT | CCCCTCCCAA | ACCACTCTCC | ACAGCTTTTT | 1560 |
| AAAAATACTT | CTACTCTTAA | CAATTACCTA | AGGTTCCTTC | AAACCCCCC  | AACTCTTAAT | 1620 |
| AGCTTCTAGT | GCTGCTACAA | TCTAAGTCAG | GTCACCAGAG | GGAAGAGAAC | ATGGCATTAA | 1680 |
| aagaatcaca | TCTTCAGAAG | AGAAGACACT | AATATTATTA | CCCATATACA | TGATTTCAGA | 1740 |
| AGATGACATA | AGATTCCTCT | TAAAGAGGAA | ATGTCAGGAA | TCAAGCCACT | GAATCCTTAA | 1800 |
| AGAGAAAAGT | TGAATATGAG | TCATTGTGTC | TGAAAACTGC | AAAGTGAACT | TAACTGAGAT | 1860 |
| CCAGCAAACA | GGTTCTGTTT | AAGAAAAATA | ATTTATACTA | AATTTAGTAA | AATGGACTTC | 1920 |
| TTATTCAAAG | CATCAATAAT | TAAAAGAATT | ATTTTAAAAA | ААААААААА  | АААААААА   | 1980 |
| TAAAAAAAA  | TCCTGCGGCC | GC         |            |            |            | 2002 |

## (2) INFORMATION FOR SEQ ID NO:6:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1322 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

| GAATTCGGCA | CGAGGGCCAC | GACTCTGCTG | GCATTTCTTC | TATAGCCACT | GGAATCTGAT | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| CCTGATTGTC | TTCCACTACT | ACCAGGCCAT | CACCACTCCG | CCTGGGTACC | CACCCCAGGG | 120 |
| CAGGAATGAT | ATCGCCACCG | TCTCCATCTG | TAAGAAGTGC | ATTTACCCCA | AGCCAGCCCG | 180 |
| AACACACCAC | TGCAGCATCT | GCAACAGGTG | TGTGCTGAAG | ATGGATCACC | ACTGCCCCTG | 240 |
| GCTAAACAAT | TGTGTGGCC  | ACTATAACCA | TCGGTACTTC | TTCTCTTTCT | GCTTTTTCAT | 300 |
| GACTCTGGGC | TGTGTCTACT | GCAGCTATGG | AAGTTGGGAC | CTTTTCCGGG | AGGCTTATGC | 360 |
| TGCCATTGAG | AAAATGAAAC | AGCTCGACAA | GAACAAACTA | CAGGCGGTTG | CCAACCAGAC | 420 |
| TTATCACCAG | ACCCCACCAC | CCACCTTCTC | CTTTCGAGAA | AGGATGACTC | ACAAGAGTCT | 480 |
| TGTCTACCTC | TGGTTCCTGT | GCAGTTCTGT | GGCACTTGCC | CTGGGTGCCC | TAACTGTATG | 540 |
| GCATGCTGTT | CTCATCAGTC | GAGGTGAGAC | TAGCATCGAA | AGGCACATCA | ACAAGAAGGA | 600 |
| GAGACGTCGG | CTACAGGCCA | AGGGCAGAGT | ATTTAGGAAT | CCTTACAACT | ACGGCTGCTT | 660 |
| GGACAACTGG | AAGGTATTCC | TGGGTGTGGA | TACAGGAAGG | CACTGGCTTA | CTCGGGTGCT | 720 |
| CTTACCTTCT | ACTCACTTGC | CCCATGGGAA | TGGAATGAGC | TGGGAGCCCC | CTCCCTGGGT | 780 |

| GACTGCTCAC | TCAGCCTCTG | TGATGGCAGT | GTGAGCTGGA | CTGTGTCAGC | CACGACTCGA | 840  |
|------------|------------|------------|------------|------------|------------|------|
| GCACTCATTC | TGCTCCCTAT | GTTATTTCAA | GGGCCTCCAA | GGGCAGCTTT | TCTCAGAATC | 900  |
| CTTGATCAAA | AAGAGCCAGT | GGGCCTGCCT | TAGGGTACCA | TGCAGGACAA | TTCAAGGACC | 960  |
| AGCCTTTTTA | CCACTGCAGA | AGAAAGACAC | AATGTGGAGA | AATCTTAGGA | CTGACATCCC | 1020 |
| TTTACTCAGG | CAAACAGAAG | TTCCAACCCC | AGACTAGGGG | TCAGGCAGCT | AGCTACCTAC | 1080 |
| CTTGCCCAGT | GCTGACCCGG | ACCTCCTCCA | GGATACAGCA | CTGGAGTTGG | CCACCACCTC | 1140 |
| TTCTACTTGC | TGTCTGAAAA | AACACCTGAC | TAGTACAGCT | GAGATCTTGG | CTTCTCAACA | 1200 |
| GGGCAAAGAT | ACCAGGCCTG | CTGCTGAGGT | CACTGCCACT | TCTCACATGC | TGCTTAAGGG | 1260 |
| AGCACAAATA | AAGGTATTCG | ATTTTTAAAA | AAAAAAAA   | TAAAAAAAT  | TCCTGCGGCC | 1320 |
| GC         |            |            |            |            |            | 1322 |

## (2) INFORMATION FOR SEQ ID NO:7:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1573 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

| GAATTCGGCA | CGAGGAGCCT. | GCCTTCATCT | AGGATGGCTC | CTCTGGGCAT | GCTGCTTGGG | 60. |
|------------|-------------|------------|------------|------------|------------|-----|
| CTGCTGATGG | CCGCCTGCTT  | CACCTTCTGC | CTCAGTCATC | AGAACCTGAA | GGAGTTTGCC | 120 |
| CTGACCAACC | CAGAGAAGAG  | CAGCACCAAA | GAAACAGAGA | GAAAAGAAAC | CAAAGCCGAG | 180 |
| GAGGAGCTGG | ATGCCGAAGT  | CCTGGAGGTG | TTCCACCCGA | CGCATGAGTG | GCAGGCCCTT | 240 |
| CAGCCAGGGC | AGGCTGTCCC  | TGCAGGATCC | CACGTACGGC | TGAATCTTCA | GACTGGGGAA | 300 |
| AGAGAGGCAA | AACTCCAATA  | TGAGGACAAG | TTCCGAAATA | ATTTGAAAGG | CAAAAGGCTG | 360 |
| GATATCAACA | CCAACACCTA  | CACATCTCAG | GATCTCAAGA | GTGCACTGGC | AAAATTCAAG | 420 |
| GAGGGGGCAG | AGATGGAGAG  | TTCAAAGGAA | GACAAGGCAA | GGCAGGCTGA | GGTAAAGCGG | 480 |
| CTCTTCCGCC | CCATTGAGGA  | ACTGAAGAAA | GACTTTGATG | AGCTGAATGT | TGTCATTGAG | 540 |
| ACTGACATGC | AGATCATGGT  | ACGGCTGATC | AACAAGTTCA | ATAGTTCCAG | CTCCAGTTTG | 600 |
| GAAGAGAAGA | TTGCTGCGCT  | CTTTGATCTT | GAATATTATG | TCCATCAGAT | GGACAATGCG | 660 |
| CAGGACCTGC | TTTCCTTTGG  | TGGTCTTCAA | GTGGTGATCA | ATGGGCTGAA | CAGCACAGAG | 720 |
| CCCCTCGTGA | AGGAGTATGC  | TGCGTTTGTG | CTGGGCGCTG | CCTTTTCCAG | CAACCCCAAG | 780 |
| GTCCAGGTGG | AGGCCATCGA  | AGGGGGAGCC | CTGCAGAAGC | TGCTGGTCAT | CCTGGCCACG | 840 |

| GAGCAGCCGC | TCACTGCAAA | GAAGAAGGTC | CTGTTTGCAC | TGTGCTCCCT | GCTGCGCCAC | 900  |
|------------|------------|------------|------------|------------|------------|------|
| TTCCCCTATG | CCCAGCGGCA | GTTCCTGAAG | CTCGGGGGGC | TGCAGGTCCT | AGGACCCTG  | 960  |
| GTGCAGGAGA | AGGGCACGGA | GGTGCTCGCC | GTGCGCGTGG | TCACACTGCT | CTACGACCTG | 1020 |
| GTCACGGAGA | AGATGTTCGC | CGAGGAGGAG | GCTGAGCTGA | CCCAGGAGAT | GTCCCCAGAG | 1080 |
| AAGCTGCAGC | AGTATCGCCA | GGTACACCTC | CTGCCAGGCC | TGTGGGAACA | GGGCTGGTGC | 1140 |
| GAGATCACGG | CCCACCTCCT | GGCGCTGCCC | GAGCATGATG | CCCGTGAGAA | GGTGCTGCAG | 1200 |
| ACACTGGGCG | TCCTCCTGAC | CACCTGCCGG | GACCGCTACC | GTCAGGACCC | CCAGCTCGGC | 1260 |
| AGGACACTGG | CCAGCCTGCA | GGCTGAGTAC | CAGGTGCTGG | CCAGCCTGGA | GCTGCAGGAT | 1320 |
| GGTGAGGACG | AGGGCTACTT | CCAGGAGCTG | CTGGGCTCTG | TCAACAGCTT | GCTGAAGGAG | 1380 |
| CTGAGATGAG | GCCCACACC  | AGGACTGGAC | TGGGATGCCG | CTAGTGAGGC | TGAGGGGTGC | 1440 |
| CAGCGTGGGT | GGGCTTCTCA | GGCAGGAGGA | CATCTTGGCA | GTGCTGGCTT | GGCCATTAAA | 1500 |
| TGGAAACCTG | AAGGCCAAAA | АААААААА   | ААААААААА  | АААААААА   | АААААААА   | 1560 |
| TTCCTGCGGC | CGC        |            |            |            |            | 1573 |

#### (2) INFORMATION FOR SEQ ID NO:8:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1185 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

| GAATTCGGCA | CGAGGGGGCT | TTAAGGGACA | GCTGAGCCGG | CAGGTGGCAG | ATCAGATGTG | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| GCAGGCTGGG | AAAAGACAAG | CCTCCAGGGC | CTTCAGCTTG | TACGCCAACA | TCGACATCCT | 120 |
| CAGACCCTAC | TTTGATGTGG | AGCCTGCTCA | GGTGCGAAGC | AGGCTCCTGG | AGTCCATGAT | 180 |
| CCCTATCAAG | ATGGTCAACT | TCCCCCAGAA | AATTGCAGGT | GAACTCTATG | GACCTCTCAT | 240 |
| GCTGGTCTTC | ACTCTGGTTG | CTATCCTACT | CCATGGGATG | AAGACGTCTG | ACACTATTAT | 300 |
| CCGGGAGGGC | ACCCTGATGG | GCACAGCCAT | TGGCACCTGC | TTCGGCTACT | GGCTGGGAGT | 360 |
| CTCATCCTTC | ATTTACTTCC | TTGCCTACCT | GTGCAACGCC | CAGATCACCA | TGCTGCAGAT | 420 |
| GTTGGCACTG | CTGGGCTATG | GCCTCTTTGG | GCATTGCATT | GTCCTGTTCA | TCACCTATAA | 480 |
| TATCCACCTC | CACGCCCTCT | TCTACCTCTT | CTGGCTGTTG | GTGGGTGGAC | TGTCCACACT | 540 |
| GCGCATGGTA | GCAGTGTTGG | TGTCTCGGAC | CGTGGGCCCC | ACACAGCGGC | TGCTCCTCTG | 600 |
| TGGCACCCTG | GCTGCCCTAC | ACATGCTCTT | CCTGCTCTAT | CTGCATTTTG | CCTACCACAA | 660 |

| AGTGGTAGAG | GGGATCCTGG | ACACACTGGA | GGGCCCCAAC | ATCCCGCCCA | TCCAGAGGGT | 720  |
|------------|------------|------------|------------|------------|------------|------|
| CCCCAGAGAC | ATCCCTGCCA | TGCTCCCTGC | TGCTCGGCTT | CCCACCACCG | TCCTCAACGC | 780  |
| CACAGCCAAA | GCTGTTGCGG | TGACCCTGCA | GTCACACTGA | CCCCACCTGA | AATTCTTGGC | 840  |
| CAGTCCTCTT | TCCCGCAGCT | GCAGAGAGGA | GGAAGACTAT | TAAAGGACAG | TCCTGATGAC | 900  |
| ATGTTTCGTA | GATGGGGTTT | GCAGCTGCCA | CTGAGCTGTA | GCTGCGTAAG | TACCTCCTTG | 960  |
| ATGCCTGTCG | GCACTTCTGA | AAGGCACAAG | GCCAAGAACT | CCTGGCCAGG | ACTGCAAGGC | 1020 |
| TCTGCAGCCA | ATGCAGAAAA | TGGGTCAGCT | CCTTTGAGAA | CCCCTCCCCA | CCTACCCCTT | 1080 |
| CCTTCCTCTT | TATCTCTCCC | ACATTGTCTT | GCTAAATATA | GACTTGGTAA | TTAAAATGTT | 1140 |
| GATTGAAGTC | TGGAAAAAA  | ААААААААА  | AATTCCTGCG | GCCGC      |            | 1185 |

#### (2) INFORMATION FOR SEQ ID NO:9:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1226 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

| GAATTCGGCA | CGAGGCAAGC | CACCATCTTC | CTTCGGCCTG | CACCCCTTTA | AAGGCACCCA | 60  |
|------------|------------|------------|------------|------------|------------|-----|
| GACCCCTCTG | GAAAAAGATG | AACTGAAGCC | CTTTGACATC | CTCCAGCCTA | AGGAGTACTT | 120 |
| CCAGCTCAGC | CGCCACACGG | TCATTAAGAT | GGGAAGTGAG | AACGAGGCCC | TGGATCTCTC | 180 |
| CATGAAGTCA | GTGCCCTGGC | TCAAGGCTGG | TGAAGTCAGT | CCCCCAATCT | TCCAGGAAGA | 240 |
| TGCAGCCCTA | GACCTGTCAG | TGGCAGCCCA | CCGGAAATCC | GAGCCTCCCC | CTGAGACACT | 300 |
| GTATGACAGT | GGTGCATCAG | TGGACAGCTC | AGGTCACACA | GTGATGGAGA | AACTTCCCAG | 360 |
| TGGCATGGAA | ATTTCTTTTG | CCCTGCCAC  | GTCCCATGAG | GCCCAGCCA  | TGATGGATAG | 420 |
| TCACATCAGC | AGCAGTGATG | CTGCTACCGA | GATGCTCAGC | CAGCCCAACC | ACCCCAGCGG | 480 |
| CGAAGTCAAG | GCTGAAAATA | ACATTGAGAT | GGTGGGCGAG | TCCCAGGCGG | CCAAGGTCAT | 540 |
| TGTCTCTGTC | GAAGATGCTG | TGCCTACCAT | ATTCTGTGGC | AAGATCAAAG | GCCTCTCAGG | 600 |
| GGTGTCCACC | AAAAACTTCT | CCTTCAAAAG | AGAAGACTCC | GTGCTTCAGG | GCTATGACAT | 660 |
| CAACAGCCAA | GGGGAAGAGT | CCATGGGAAA | TGCAGAGCCC | CTTAGGAAAC | CCATCAAAAA | 720 |
| CCGGAGCATA | AAGTTAAAGA | AAGTGAACTC | CCAGGAAGTA | CACATGCTCC | CAATCAAAAA | 780 |
| ACAACGGCTG | GCCACCTTTT | TTCCAAGAAA | GTAAATAACG | GCTTTTTAAA | ATTTGTATGA | 840 |
| TTATAATATG | GGGAAAGGTG | CATTGGTTTT | ATAAAAAGGC | ATTTAAAACA | AATTATCTTT | 900 |

| GTTAATTATT | TTGGGGAGTA | GTTGGGAAAT | GGAAAGGTGA | ATTGGCTCTA | GAGGCCCTGT | 960  |
|------------|------------|------------|------------|------------|------------|------|
| ATGCTAGTAT | CATTTTCTTT | TTTAATTTTT | GACTTTTCAC | AAATGAGTAA | ATAAGAGCAA | 1020 |
| CCTATTTTTC | AAGCAGATTG | CACATTTTTT | GCAGCTTTAA | TGGAATATTG | GGTGAATTAG | 1080 |
| AGGGGTAAAA | AAAGCTATTT | TCATTGCCAC | AAAGTGCTTT | GATGATGTAA | TACCTAATAA | 1140 |
| AGGGTAGGAT | GAATATTTCA | CAATAAATGT | TTGTTTGCAC | талалалаа  | AAAAAAAA   | 1200 |
| ААААААААА  | AAATTCCTGC | GGCCGC     |            |            |            | 1226 |

## (2) INFORMATION FOR SEQ ID NO:10:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1049 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

| GAATTCGGCA | CGAGGGCGCC | ATGGTGAAGG | TGACGTTCAA | CTCCGCTCTG | GCCCAGAAGG | 60   |
|------------|------------|------------|------------|------------|------------|------|
| AGGCCAAGAA | GGACGAGCCC | AAGAGCGGCG | AGGAGGCGCT | CATCATCCCC | CCCGACGCCG | 120  |
| TCGCGGTGGA | CTGCAAGGAC | CCAGATGATG | TGGTACCAGT | TGGCCAAAGA | AGAGCCTGGT | 180  |
| GTTGGTGCAT | GTGCTTTGGA | CTAGCATTTA | TGCTTGCAGG | TGTTATTCTA | GGAGGAGCAT | 240  |
| ACTTGTACAA | ATATTTTGCA | CTTCAACCAG | ATGACGTGTA | CTACTGTGGA | ATAAAGTACA | 300- |
| TCAAAGATGA | TGTCATCTTA | AATGAGCCCT | CTGCAGATGC | CCCAGCTGCT | CTCTACCAGA | 360  |
| CAATTGAAGA | AAATATTAAA | ATCTTTGAAG | AAGAAGAAGT | TGAATTTATC | AGTGTGCCTG | 420  |
| TCCCAGAGTT | TGCAGATAGT | GATCCTGCCA | ACATTGTTCA | TGACTTTAAC | AAGAAACTTA | 480  |
| CAGCCTATTT | AGATCTTAAC | CTGGATAAGT | GCTATGTGAT | CCCTCTGAAC | ACTTCCATTG | 540  |
| TTATGCCACC | CAGAAACCTA | CTGGAGTTAC | TTATTAACAT | CAAGGCTGGA | ACCTATTTGC | 600  |
| CTCAGTCCTA | TCTGATTCAT | GAGCACATGG | TTATTACTGA | TCGCATTGAA | AACATTGATC | 660  |
| ACCTGGGTTT | CTTTATTTAT | CGACTGTGTC | ATGACAAGGA | AACTTACAAA | CTGCAACGCA | 720  |
| GAGAAACTAT | TAAAGGTATT | CAGAAACGTG | AAGCCAGCAA | TTGTTTCGCA | ATTCGGCATT | 780  |
| TTGAAAACAA | ATTTGCCGTG | GAAACTTTAA | TTTGTTCTTG | AACAGTCAAG | AAAAACATTA | 840  |
| TTGAGGAAAA | TTAATATCAC | AGCATAACCC | CACCCTTTAC | ATTTTGTTGC | AGTTGATTAT | 900  |
| TTTTTAAAGT | CTTCTTTCAT | GTAAGTAGCA | AACAGGGCTT | TACTATCTTT | TCATCTCATT | 960  |
| AATTCAATTA | AAACCATTAC | CTTAAAAAAA | АААААААА   | АААААААА   | ААААААААА  | 1020 |
| ААААААААА  | AAAAAATTCC | TGCGGCCGC  |            |            |            | 1049 |

## (2) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1142 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

| GAATTCGGCA | CGAGGGGAGA | ATACTTTTTG | CGATGCCTAC | TGGAGACTTT | GATTCGAAGC | 60   |
|------------|------------|------------|------------|------------|------------|------|
| CCAGTTGGGC | CGACCAGGTG | GAGGAGGAGG | GGGAGGACGA | CAAATGTGTC | ACCAGCGAGC | 120  |
| TCCTCAAGGG | GATCCCTCTG | GCCACAGGTG | ACACCAGCCC | AGAGCCAGAG | CTACTGCCGG | 180  |
| GAGCTCCACT | GCCGCCTCCC | AAGGAGGTCA | TCAACGGAAA | CATAAAGACA | GTGACAGAGT | 240  |
| ACAAGATAGA | TGAGGATGGC | AAGAAGTTCA | AGATTGTCCG | CACCTTCAGG | ATTGAGACCC | 300  |
| GGAAGGCTTC | AAAGGCTGTC | GCAAGGAGGA | AGAACTGGAA | GAAGTTCGCG | AACTCAGAGT | 360  |
| TTGACCCCCC | CGGACCCAAT | GTGGCCACCA | CCACTGTCAG | TGACGATGTC | TCTATGACGT | 420  |
| TCATCACCAG | CAAAGAGGAC | CTGAACTGCC | AGGAGGAGGA | GGACCCTATG | AACAAATTCA | 480  |
| AGGGCCAGAA | GATCGTGTCC | TGCCGCATCT | GCAAGGGCGA | CCACTGGACC | ACCCGCTGCC | 540  |
| CCTACAAGGA | TACGCTGGGG | CCCATGCAGA | AGGAGCTGGC | CGAGCAGCTG | GGCCTGTCTA | 600  |
| CTGGCGAGAA | GGAGAAGCTG | CCGGGAGAGC | TAGAGCCGGT | GCAGGCCACG | CAGAACAAGA | 660  |
| CAGGGAAGTA | TGTGCCGCCG | AGCCTGCGCG | ACGGGGCCAG | CCCCCCCGG  | GAGTCCATGC | 720  |
| AGCCCAACCG | CAGAGCCGAC | GACAACGCCA | CCATCCGTGT | CACCAACTTG | CGCAGAGGAC | 780  |
| ACGCGTGAGA | CCGACCTGCA | GGAGCTCTTC | CGGCCTTTCG | GCTCCATCTC | CCGCATCTAC | 840  |
| CTGGCTAAGG | ACAAGACCAC | TGGCCAATCC | AAGGGCTTTG | CCTTCATCAG | CTTCCACCGC | 900  |
| CGCGAGGATG | CTGCGCGTGC | CATTGCCGGG | GTGTCCGGCT | TTGGCTACGA | CCACCTCATC | 960  |
| CTCAACGTCG | AGTGGGCCAA | GCCGTCCACC | AACTAAGCCA | GCTGCCACTG | TGTACTCGGT | 1020 |
| CCGGGACCCT | TGGCGACAGA | AGACAGCCTC | CGAGAGCGCG | GGCTCCAAGG | GCAATAAAGC | 1080 |
| AGCTCCACTC | TCAAAAAAA  | АААААААА   | ААААААААА  | AAAAAAAAT  | TCCTGCGGCC | 1140 |
| GC         |            |            |            |            |            | 1142 |

- (2) INFORMATION FOR SEQ ID NO:12:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1696 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

| GAATTCGGCA | CGAGGGAAAC | ATGGCGGTAG | GCTGGGACCA | TAACACAAGC | ATGACTATAT | 60   |
|------------|------------|------------|------------|------------|------------|------|
| GAAGGAAGAG | GAAGGTTTTC | CTGAAGATGA | GGCGACTGAA | TCGGAAAAA  | ACTTTAAGTT | 120  |
| TGGTAAAAGA | GTTGGATGCC | TTTCCGAAGG | TTCCTGAGAG | CTATGTAGAG | ACTTCAGCCA | 180  |
| GTGGAGGTAC | AGTTTCTCTA | ATAGCATTTA | CAACTATGGC | TTTATTAACC | ATAATGGAAT | 240  |
| TCTCAGTATA | TCAAGATACA | TGGATGAAGT | ATGAATACGA | AGTAGACAAG | GATTTTTCTA | 300  |
| GCAAATTAAG | AATTAATATA | GATATTACTG | TTGCCATGAA | GTGTCAATAT | GTTGGAGCGG | 360  |
| ATGTATTGGA | TTTAGCAGAA | ACAATGGTTG | CATCTGCAGA | TGGTTTAGTT | TATGAACCAA | 420  |
| CAGTATTTGA | TCTTTCACCA | CAGCAGAAAG | AGTGGCAGAG | GATGCTGCAG | CTGATTCAGA | 480  |
| GTAGGCTACA | AGAAGAGCAT | TCACTTCAAG | ATGTGATATT | TAAAAGTGCT | TTTAAAAGTA | 540  |
| CATCAACAGC | TCTTCCACCA | AGAGAAGATG | ATTCATCACA | GTCTCCAAAT | GCATGCAGAA | 600  |
| TTCATGGCCA | TCTATATGTC | AATAAAGTAG | CAGGGAATTT | TCACATAACA | GTGGGCAAGG | 660  |
| CAATTCCACA | TCCTCGTGGT | CATGCACATT | TGGCAGCACT | TGTCAACCAT | GAATCTTACA | 720  |
| ATTTTTCTCA | TAGAATAGAT | CATTTGTCTT | TTGGAGAGCT | TGTTCCAGCA | ATTATTAATC | 780  |
| CTTTAGATGG | AACTGAAAAA | ATTGCTATAG | ATCACAACCA | GATGTTCCAA | TATTTTATTA | 840  |
| CAGTTGTGCC | AACAAAACTA | CATACATATA | AAATATCAGC | AGACACCCAT | CAGTTTTCTG | 900  |
| TGACAGAAAG | GGAACGTATC | ATTAACCATG | CTGCAGGCAG | CCATGGAGTC | TCTGGGATAT | 960  |
| TTATGAAATA | TGATCTCAGT | TCTCTTATGG | TGACAGTTAC | TGAGGAGCAC | ATGCCATTCT | 1020 |
| GGCAGTTTTT | TGTAAGACTC | TGTGGTATTG | TTGGAGGAAT | CTTTTCAACA | ACAGGCATGT | 1080 |
| TACATGGAAT | TGGAAAATTT | ATAGTTGAAA | TAATTTGCTG | TCGTTTCAGA | CTTGGATCCT | 1140 |
| ATAAACCTGT | CAATTCTGTT | CCTTTTGAGG | ATGGCCACAC | AGACAACCAC | TTACCTCTTT | 1200 |
| TAGAAAATAA | TACACATTAA | CACCTCCCGA | TTGAAGGAGA | AAAACTTTTT | GCCTGAGACA | 1260 |
| TAAAACCTTT | TTTTAATAAT | AAAATATTGT | GCAATATATT | CAAAGAAAAG | AAAACACAAA | 1320 |
| TAAGCAGAAA | ACATACTTAT | TTTAAAAAAG | AAAAAAAAGG | АТАААААААС | CCAAACTGAA | 1380 |
| ATTCTATATA | CGTTGTGTCT | GTTACAAATG | TCGTAGAAGA | AATCATGCAG | CTAAACGATG | 1440 |
| AAGAAGCCCA | ACTGGAGTGT | TGCTTTGAAG | ATGACGCCTT | CTTATATTTT | CATAGCAAAT | 1500 |
| GGGTGGTATC | AAAATCAGAC | ATTGCTTCTT | GCTGATAAAA | AGCCTGAAGG | AAATAAGTGA | 1560 |
| AACTACATCT | ATGGGAAAAA | AAAAAACATT | GAGAAGTGCA | AATGTTCGCA | TCCTTTTGTT | 1620 |
| TTTAAAAGAT | ATGATGTCAG | AATAAAATGT | GGAAAACATA | CGGAAAAAA  | АААААААА   | 1680 |
| AAATTCCTGC | GGCCGC     |            |            |            |            | 1696 |

#### (2) INFORMATION FOR SEQ ID NO:13:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1100 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

|            |            |            |            | •          |            |      |
|------------|------------|------------|------------|------------|------------|------|
| GAATTCGGCA | CGAGGCGGCA | CGAGGCGGCA | CGAGGGTGGC | ATATCACGGC | CATGGGGTCT | 60   |
| CAGCATTCCG | CTGCTGCTCG | CCCCTCCTCC | TGCAGGCGAA | AGCAAGAAGA | TGACAGGGAC | 120  |
| GGTTTGCTGG | CTGAACGAGA | GCAGGAAGAA | GCCATTGCTC | AGTTCCCATA | TGTGGAATTC | 180  |
| ACCGGGAGAG | ATAGCATCAC | CTGTCTCACG | TGCCAGGGGA | CAGGCTACAT | TCCAACAGAG | 240  |
| CAAGTAAATG | AGTTGGTGGC | TTTGATCCCA | CACAGTGATC | AGAGATTGCG | CCCTCAGCGA | 300  |
| ACTAAGCAAT | ATGTCCTCCT | GTCCATCCTG | CTTTGTCTCC | TGGCATCTGG | TTTGGTGGTT | 360  |
| TTCTTCCTGT | TTCCGCATTC | AGTCCTTGTG | GATGATGACG | GCATCAAAGT | GGTGAAAGTC | 420  |
| ACATTTAATA | AGCAAGACTC | CCTTGTAATT | CTCACCATCA | TGGCCACCCT | GAAAATCAGG | 480  |
| AACTCCAACT | TCTACACGGT | GGCAGTGACC | AGCCTGTCCA | GCCAGATTCA | GTACATGAAC | 540  |
| ACAGTGGTCA | GTACATATGT | GACTACTAAC | GTCTCCCTTA | TTCCACCTCG | GAGTGAGCAA | 600  |
| CTGGTGAATT | TTACCGGGAA | GGCCGAGATG | GGAGGACCGT | TTTCCTATGT | GTACTTCTTC | 660  |
| TGCACGGTAC | CTGAGATCCT | GGTGCACAAC | ATAGTGATCT | TCATGCGAAC | TTCAGTGAAG | 720  |
| ATTTCATACA | TTGGCCTCAT | GACCCAGAGC | TCCTTGGAGA | CACATCACTA | TGTGGATTGT | 780  |
| GGAGGAAATT | CCACAGCTAT | TTAACAACTG | CTATTGGTTC | TTCCACACAG | CGCCTGTAGA | 840  |
| AGAGAGCACA | GCATATGTTC | CCAAGGCCTG | AGTTCTGGAC | CTACCCCCAC | GTGGTGTAAG | 900  |
| CAGAGGAGGA | ATTGGTTCAC | TTAACTCCCA | GCAAACATCC | TCCTGCCACT | TAGGAGGAAA | 960  |
| CACCTCCCTA | TGGTACCATT | TATGTTTCTC | AGAACCAGCA | GAATCAGTGC | CTAGCCTGTG | 1020 |
| CCCAGCAAAT | AGTTGGCACT | CAATAAAGAT | TTGCAGAATT | TAAAAAAAA  | ААААААААА  | 1080 |
| AAAAAAATTC | CTGCGGCCGC |            |            |            |            | 1100 |

## (2) INFORMATION FOR SEQ ID NO:14:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1588 base pairs
  - (B) TYPE: nucleic acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

| GAATTCGGCA | CGAGGGTACC | TGCTTTTCTA | TTGCCTCTTT | GAAACAATGG | TCACGTGTTT | 60   |
|------------|------------|------------|------------|------------|------------|------|
| CCATGTTCCC | TACTCGGCTC | TCACCATGTT | CATCAGCACC | GAGCAGACTG | AGCGGGATTC | 120  |
| TGCCACCGCC | TATCGGATGA | CTGTGGAAGT | GCTGGGCACA | GTGCTGGGCA | CGGCGATCCA | 180  |
| GGGACAAATC | GTGGGCCAAG | CAGACACGCC | TTGTTTCCAG | GACCTCAATA | GCTCTACAGT | 240  |
| AGCTTCACAA | AGTGCCAACC | ATACACATGG | CACCACCTCA | CACAGGGAAA | CGCAAAAGGC | 300  |
| ATACCTGCTG | GCAGCGGGG  | TCATTGTCTG | TATCTATATA | ATCTGTGCTG | TCATCCTGAT | 360  |
| CCTGGGCGTG | CGGGAGCAGA | GAGAACCCTA | TGAAGCCCAG | CAGTCTGAGC | CAATCGCCTA | 420  |
| CTTCCGGGGC | CTACGGCTGG | TCATGAGCCA | CGGCCCATAC | ATCAAACTTA | TTACTGGCTT | 480  |
| CCTCTTCACC | TCCTTGGCTT | TCATGCTGGT | GGAGGGGAAC | TTTGTCTTGT | TTTGCACCTA | 540  |
| CACCTTGGGC | TTCCGCAATG | AATTCCAGAA | TCTACTCCTG | GCCATCATGC | TCTCGGCCAC | 600  |
| TTTAACCATT | CCCATCTGGC | AGTGGTTCTT | GACCCGGTTT | GGCAAGAAGA | CAGCTGTATA | 660  |
| TGTTGGGATC | TCATCAGCAG | TGCCATTTCT | CATCTTGGTG | GCCCTCATGG | AGAGTAACCT | 720  |
| CATCATTACA | TATGCGGTAG | CTGTGGCAGC | TGGCATCAGT | GTGGCAGCTG | CCTTCTTACT | 780  |
| ACCCTGGTCC | ATGCTGCCTG | ATGTCATTGA | CGACTTCCAT | CTGAAGCAGC | CCCACTTCCA | 840  |
| TGGAACCGAG | CCCATCTTCT | TCTCCTTCTA | TGTCTTCTTC | ACCAAGTTTG | CCTCTGGAGT | 900  |
| GTCACTGGGC | ATTTCTACCC | TCAGTCTGGA | CTTTGCAGGG | TACCAGACCC | GTGGCTGCTC | 960  |
| GCAGCCGGAA | CGTGTCAAGT | TTACACTGAA | CATGCTCGTG | ACCATGGCTC | CCATAGTTCT | 1020 |
| CATCCTGCTG | GGCCTGCTGC | TCTTCAAAAT | GTACCCCATT | GATGAGGAGA | GGCGGCGCA  | 1080 |
| GAATAAGAAG | GCCCTGCAGG | CACTGAGGGA | CGAGGCCAGC | AGCTCTGGCT | GCTCAGAAAC | 1140 |
| AGACTCCACA | GAGCTGGCTA | GCATCCTCTA | GGGCCCGCCA | CGTTGCCCGA | AGCCACCATG | 1200 |
| CAGAAGGCCA | CAGAAGGGAT | CAGGACCTGT | CTGCCGGCTT | GCTGAGCAGC | TGGACTGCAG | 1260 |
| GTGCTAGGAA | GGGAACTGAA | GACTCAAGGA | GGTGGCCCAG | GACACTTGCT | GTGCTCACTG | 1320 |
| TGGGGCCGGC | TGCTCTGTGG | CCTCCTGCCT | CCCCTCTGCC | TGCCTGTGGG | GCCAAGCCCT | 1380 |
| GGGGCTGCCA | CTGTGAATAT | GCCAAGGACT | GATCGGGCCT | AGCCCGGAAC | ACTAATGTAG | 1440 |
| AAACCTTTTT | TTTACAGAGC | CTAATTAATA | ACTTAATGAC | TGTGTACATA | GCAATGTGTG | 1500 |
| TGTATGTATA | TGTCTGTGAG | CTATTAATGT | TATTAATTTT | CATAAAAGCT | GGAAAGCAAA | 1560 |
| ААААААААА  | AAAAATTCCT | GCGGCCGC   |            |            |            | 1588 |

## (2) INFORMATION FOR SEQ ID NO:15:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1535 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

| GAATTCGGCA | CGAGGCGGAA | GTCCCGTCTC | ACGGTTGCCC | TGGCAGCGCG | CGAGGCTGGT | 60   |
|------------|------------|------------|------------|------------|------------|------|
| GAGTCGGCAG | CCCTGTGGCA | GCCGGCGGC  | TGGTTTCCAT | GGTTGCACGA | TTAGGAACCA | 120  |
| CCAGCTGCTG | CATCCCATGG | CCAGGGGTGG | CGTCCAGGTG | GCAGAGCAGC | TAGGAACGCA | 180  |
| AGGCCTGAAC | CTGGGGCCAG | ACACCCTGCT | CTCCCGGCCA | TGGTCAACGA | CCCTCCAGTA | 240  |
| CCTGCCTTAC | TGTGGGCCCA | GGAGGTGGGC | CAAGTCTTGG | CAGGCCGTGC | CCGCAGGCTG | 300  |
| CTGCTGCAGT | TTGGGGTGCT | CTTCTGCACC | ATCCTCCTTT | TGCTCTGGGT | GTCTGTCTTC | 360  |
| CTCTATGGCT | CCTTCTACTA | TTCCTATATG | CCGACAGTCA | GCCACCTCAG | CCCTGTGCAT | 420  |
| TTCTACTACA | GGACCGACTG | TGATTCCTCC | ACCACCTCAC | TCTGCTCCTT | CCCTGTTGCC | 480  |
| AATGTCTCGC | TGACTAAGGG | TGGACGTGAT | CGGGTGCTGA | TGTATGGACA | GCCGTATCGT | 540  |
| GTTACCTTAG | AGCTTGAGCT | GCCAGAGTCC | CCTGTGAATC | AAGATTTGGG | CATGTTCTTG | 600  |
| GTCACCATTT | CCTGCTACAC | CAGAGGTGGC | CGAATCATCT | CCACTTCTTC | GCGTTCGGTG | 660  |
| ATGCTGCATT | ACCGCTCAGA | CCTGCTCCAG | ATGCTGGACA | CACTGGTCTT | CTCTAGCCTC | 720  |
| CTGCTATTTG | GCTTTGCAGA | GCAGAAGCAG | CTGCTGGAGG | TGGAACTCTA | CGCAGACTAT | 780  |
| AGAGAGAACT | CGTACGTGCC | GACCACTGGA | GCGATCATTG | AGATCCACAG | CAAGCGCATC | 840  |
| CAGCTGTATG | GAGCCTACCT | CCGCATCCAC | GCGCACTTCA | CTGGGCTCAG | ATACCTGCTA | 900  |
| TACAACTTCC | CGATGACCTG | CGCCTTCATA | GGTGTTGCCA | GCAACTTCAC | CTTCCTCAGC | 960  |
| GTCATCGTGC | TCTTCAGCTA | CATGCAGTGG | GTGTGGGGGG | GCATCTGGCC | CCGACACCGC | 1020 |
| TTCTCTTTGC | AGGTTAACAT | CCGAAAAAGA | GACAATTCCC | GGAAGGAAGT | CCAACGAAGG | 1080 |
| ATCTCTGCTC | ATCAGCCAGG | GCCTGAAGGC | CAGGAGGAGT | CAACTCCGCA | ATCAGATGTT | 1140 |
| ACAGAGGATG | GTGAGAGCCC | TGAAGATCCC | TCAGGGACAG | AGGTCAGCTG | TCCGAGGAGG | 1200 |
| AGAAACCAGA | TCAGCAGCCC | CTGAGCGGAG | AAGAGGAGCT | AGAGCCTGAG | GCCAGTGATG | 1260 |
| GTTCAGGCTC | CTGGGAAGAT | GCAGCTTTGC | TGACGGAGGC | CAACCTGCCT | GCTCCTGCTC | 1320 |
| CTGCTTCTGC | TTCTGCCCCT | GTCCTAGAGA | CTCTGGGCAG | CTCTGAACCT | GCTGGGGGTG | 1380 |
| CTCTCCGACA | GCGCCCCACC | TGCTCTAGTT | CCTGAAGAAA | AGGGGCAGAC | TCCTCACATT | 1440 |
| CCAGCACTTT | CCCACCTGAC | TCCTCTCCCC | TCGTTTTTCC | TTCAATAAAC | TATTTTGTGT | 1500 |
| СААААААА   | алалалала  | AATTCCTGCG | GCCGC      |            |            | 1535 |

## (2) INFORMATION FOR SEQ ID NO:16:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1322 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

| GAATTCGGCA | CGAGGGCGGG | CGCTACGGGC | TTGACTCCCC | CAAGGCCGAG | GTCCGCGGCC | 60   |
|------------|------------|------------|------------|------------|------------|------|
| AGGTGCTGGC | GCCGCTGCCC | CTCCACGGAG | TTGCTGATCA | TCTGGGCTGT | GATCCACAAA | 120  |
| CCCGGTTCTT | TGTCCCTCCT | AATATCAAAC | AGTGGATTGC | CTTGCTGCAG | AGGGGAAACT | 180  |
| GCACGTTTAA | AGAGAAAATA | TCACGGGCCG | CTTTCCACAA | TGCAGTTGCT | GTAGTCATCT | 240  |
| ACAATAATAA | ATCCAAAGAG | GAGCCAGTTA | CCATGACTCA | TCCAGGCACT | GGAGATATTA | 300  |
| TTGCTGTCAT | GATAACAGAA | TTGAGGGGTA | AGGATATTTT | GAGTTATCTG | GAGAAAAACA | 360  |
| TCTCTGTACA | AATGACAATA | GCTGTTGGAA | CTCGAATGCC | ACCGAAGAAC | TTCAGCCGTG | 420  |
| GCTCTCTAGT | CTTCGTGTCA | ATATCCTTTA | TTGTTTTGAT | GATTATTTCT | TCAGCATGGC | 480  |
| TCATATTCTA | CTTCATTCAA | AAGATCAGGT | ACACAAATGC | ACGCGACAGG | AACCAGCGTC | 540  |
| GTCTCGGAGA | TGCAGCCAAG | AAAGCCATCA | GTAAATTGAC | AACCAGGACA | GTAAAGAAGG | 600  |
| GTGACAAGGA | AACTGACCCA | GACTTTGATC | ATTGTGCAGT | CTGCATAGAG | AGCTATAAGC | 660  |
| AGAATGATGT | CGTCCGAATT | CTCCCTGCA  | AGCATGTTTT | CCACAAATCC | TGCGTGGATC | 720  |
| CCTGGCTTAG | TGAACATTGT | ACCTGTCCTA | TGTGCAAACT | TAATATATTG | AAGGCCCTGG | 780  |
| GAATTGTGCC | GAATTTGCCA | TGTACTGATA | ACGTAGCATT | CGATATGGAA | AGGCTCACCA | 840  |
| GAACCCAAGC | TGTTAACCGA | AGATCAGCCC | TCGGCGACCT | CGCCGGCGAC | AACTCCCTTG | 900  |
| GCCTTGAGCC | ACTTCGAACT | TCGGGGATCT | CACCTCTTCC | TCAGGATGGG | GAGCTCACTC | 960  |
| CGAGAACAGG | AGAAATCAAC | ATTGCAGTAA | CAAAAGAATG | GTTTATTATT | GCCAGTTTTG | 1020 |
| GCCTCCTCAG | TGCCCTCACA | CTCTGCTACA | TGATCATCAG | AGCCACAGCT | AGCTTGAATG | 1080 |
| CTAATGAGGT | AGAATGGTTT | TGAAGAAGAA | AAAACCTGCT | TTCTGACTGA | TTTTGCCTTG | 1140 |
| AAGGAAAAA  | GAACCTATTT | TTGTGCATCA | TTTACCAATC | ATGCCACACA | AGCATTTATT | 1200 |
| TTTAGTACAT | TTTATTTTTT | CATAAAATTG | CTAATGCCAA | AGCTTTGTAT | TAAAAGAAAT | 1260 |
| AAATAATAAA | ATAAAAAAAA | АААААААА   |            | TĄAAAAAA   | TCCTGCGGCC | 1320 |
| GC         |            |            |            |            | •          | 1322 |
|            |            |            |            |            |            |      |

### (2) INFORMATION FOR SEQ ID NO:17:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1711 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

| GAATTCGGCA | CGAGGCCCTC | CCGCGCTCCC | GGGGCGCGCG | GCCGCGCCC  | CCGACGCCCT | 60    |
|------------|------------|------------|------------|------------|------------|-------|
| ACATATACTC | AGGTGCGCCC | CACCTGTCCG | CCCGCACCTG | CTGGCTCACC | TCCGAGCCAC | 120   |
| CTCTGCTGCG | CACCGCAGCC | TCGGACCTAC | AGCCCAGGAT | ACTTTGGGAC | TTGCCGGCGC | 180   |
| TCAGAAACGC | GCCCAGACGG | CCCTCCACC  | TTTTGTTTGC | CTAGGGTCGC | CGAGAGCGCC | 240   |
| CGGAGGGAAC | CGCCTGGCCT | TCGGGGACCA | CCAATTTTGT | CTGGAACCAC | CCTCCCGGCG | 300   |
| TATCCTACTC | CCTGTGCCGC | GAGGCCATCG | CTTCACTGGA | GGGGTCGATT | TGTGTGTAGT | 360   |
| TTGGTGACAA | GATTTGCATT | CACCTGGCCC | AAACCCTTTT | TGTCTCTTTG | GGTGACCGGA | 420   |
| AAACTCCACC | TCAAGTTTTC | TTTTGTGGGG | CTGCCCCCA  | AGTGTCGTTT | GTTTTACTGT | 480   |
| AGGGTCTCCC | GCCCGCCCC  | CCCAGTGTTT | TCTGAGGGCG | GAAATGGCCA | ATTCGGGCCT | 540   |
| GCAGTTGCTG | GGCTTCTCCA | TGGCCCTGCT | GGGCTGGGTG | GGTCTGGTGG | CCTGCACCGC | 600   |
| CATCCCGCAG | TGGCAGATGA | GCTCCTATGC | GGGTGACAAC | ATCATCACGG | CCCAGGCCAT | 660   |
| GTACAAGGGG | CTGTGGATGG | ACTGCGTCAC | GCAGAGCACG | GGGATGATGA | GCTGCAAAAT | 720   |
| GTACGACTCG | GTGCTCGCCC | TGTCCGCGGC | CTTGCAGGCC | ACTCGAGCCC | TAATGGTGGT | 780   |
| CTCCCTGGTG | CTGGGCTTCC | TGGCCATGTT | TGTGGCCACG | ATGGGCATGA | AGTGCACGCG | . 840 |
| CTGTGGGGGA | GACGACAAAG | TGAAGAAGGC | CCGTATAGCC | ATGGGTGGAG | GCATAATTTT | 900   |
| CATCGTGGCA | GGTCTTGCCG | CCTTGGTAGC | TTGCTCCTGG | TATGGCCATC | AGATTGTCAC | 960   |
| AGACTTTTAT | AACCCTTTGA | TCCCTACCAA | CATTAAGTAT | GAGTTTGGCC | CTGCCATCTT | 1020  |
| TATTGGCTGG | GCAGGGTCTG | CCCTAGTCAT | CCTGGGAGGT | GCACTGCTCT | CCTGTTCCTG | 1080  |
| TCCTGGGAAT | GAGAGCAAGG | CTGGGTACCG | TGCACCCCGC | TCTTACCCTA | AGTCCAACTC | 1140  |
| TTCCAAGGAG | TATGTGTGAC | CTGGGATCTC | CTTGCCCCAG | CCTGACAGGC | TATGGGAGTG | 1200  |
| TCTAGATGCC | TGAAAGGGCC | TGGGGCTGAG | CTCAGCCTGT | GGGCAGGGTG | CCGGACAAAG | 1260  |
| GCCTCCTGGT | CACTCTGTCC | CTGCACTCCA | TGTATAGTCC | TCTTGGGTTG | GGGGTGGGG  | 1320  |
| GGTGCCGTTG | GTGGGAGAGA | CAAAAAGAGG | GAGAGTGTGC | TTTTTGTACA | GTAATAAAA  | 1380  |
| ATAAGTATTG | GGAAGCAGGC | TTTTTTCCCT | TCAGGGCCTC | TGCTTTCCTC | CCGTCCAGAT | 1440  |
| CCTTGCAGGG | AGCTTGGAAC | CTTAGTGCAC | CTACTTCAGT | TCAGAACACT | TAGCACCCCA | 1500  |
| CTGACTCCAC | TGACAATTGA | CTAAAAGATG | CAGGTGCTCG | TATCTCGACA | TTCATTCCCA | 1560  |
| CCCCCTCTT  | ATTTAAATAG | CTACCAAAGT | ACTTCTTTTT | TAATAAAAA  | ATAAAGATTT | 1620  |

#### 

#### (2) INFORMATION FOR SEQ ID NO:18:

#### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1553 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

| 60   | GAGGAAGGAA | GAGTGGAAGC | AGTCACTGAA | TCCAGAGTAA | CGAGGGCAGG | GAATTCGGCA |
|------|------------|------------|------------|------------|------------|------------|
| 120  | TGCCGGGGCT | CGATGCCTCC | GGGGCTGGGA | TGCGGACCGC | AGACCTCAGC | CAGGATGATT |
| 180  | CCCAGCCCTC | AAGCTACATA | CGGGGCTGAA | TCCTCTGGGC | CTGGTGCCCG | GCTGCTGCTC |
| 240  | CGCTGGGGAC | CCCACCTGCG | CCCCCCCTG  | CCACGCGCTG | GTCTGCCAGC | CTGCCCGCG  |
| 300  | AGCGTGAAGT | CCCGCGGCCG | CCGCGTCTGC | GCCGCTGTTG | TTCGACCTGT | CACGCCGGTG |
| 360  | AGCCGCTGCG | CAGTGCCTCC | CCCGGGGCTG | AACCGTGCGC | GCGCAGGGCC | CTGCGGCGGG |
| 420  | GCGGCAGCGA | GGGGCCGTGT | GACGCTGGGA | GCGGTTGCCC | CCCAGCACCT | CCCCGGGTTC |
| 480  | CGCGCCGCCT | AACCGCGCCG | CCGGGCCGAA | TGTGCGCGCT | TACCCCAGCA | CAGGCGCACC |
| 540, | GGACCAGAAG | GGGGATACAG | GGGGAACTGC | CTGTGCAGTG | CCGGCCGTGC | GGGCAAGGTC |
| 600  | AGGTGGCGCC | GTGGTGGAGA | CATCGCCGCG | ATTACAACTT | CTCAGGAGGA | CGCAGGCCCG |
| 660  | TTGTTCCTGT | GGCAGCAGGC | GTTACTTCAC | TGTGGGGCAG | CACGTGCAGC | ATCGGTGGTT |
| 720  | ATGCCCATGT | ATTATTACCA | GGACGGGCTC | TAGTGTCTGA | TCTGGGTTCA | GTACAGTGGC |
| 780  | ATGAAGCTGT | GGGGCCCGTT | GCTCCAGAAT | TTGAGGTGGT | CAGCAGTGGA | TGTCAGGAAC |
| 840  | CAAATGCTGA | AAGATTGAAT | TGCGGTGATT | AATTGGATCT | ATTGACCTTA | TGTCAAGGAT |
| 900  | TTGTGGTGGC | GCTGGAGAGT | TGACCTTCGG | GAAGATCATC | CTGATGCTGG | ACTTCCTGTA |
| 960  | GCACCAAACA | GGAATTGTCA | AGCTACTGCA | TGCAGAACAC | CCATTTTCTC | TTTGGGCAGC |
| 1020 | AGATTGATGC | GACTACGTCC | TTCAGATATG | GGATGAAGGA | AAAGAACTGG | GCGAGGGGC  |
| 1080 | ATGTGATTGG | TTGGATGGTG | TCTGGTGAAC | CTGGTGGTCC | TATGGGAATT | CACAATTAAC |
| 1140 | ATCGAGTTAG | ATTCCTTCAG | CTCCTTTGCA | CTGATGGAAT | TTGAGGGTGA | CGTCAATTCA |
| 1200 | CAAATAAGAA | AAGGCGTTTT | GATGAAAGGA | ATGAGCACCA | GCAGAATACC | GCAGTTCTTG |
| 1260 | TGAAAATGCA | AGTGAAGAAT | TGTGCCCCTT | TGTCCCTCAC | CTGCAAATGC | ATATCTGGGT |
| 1320 | TTGAAGGAAC | TGTAAAGTGG | GGTTTATGTA | TGAGTTCTGG | TTCCCTGATG | TTATCCAGAT |

| AGCTGCTCAA | AGCTCTGGAT | TGAGAGATCA | CGATGTAATT | GTCAACATAA | ATGGGAAACC | 1380 |
|------------|------------|------------|------------|------------|------------|------|
| TATTACTACT | ACAACTGATG | TTGTTAAAGC | TCTTGACAGT | GATTCCCTTT | CCATGGCTGT | 1440 |
| TCTTCGGGGA | AAAGATAATT | TGCTCCTGAC | AGTCATACCT | GAAACAATCA | ATTAAATATC | 1500 |
| TTGTTTTAAA | GTGGGATTAT | СТААААААА  | AAAAAAAAA  | TTCCTGCGGC | CGC        | 1553 |

#### (2) INFORMATION FOR SEQ ID NO:19:

# (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1596 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: cDNA

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

| 60   | ATCGCAGCCG | AGAGGCTGCA          | GCCCGGCCGT  | CGCTCCCGGA | CGAGGGGAGC | GAATTCGGCA   |
|------|------------|---------------------|-------------|------------|------------|--------------|
| 120  | CAGGCCGCGC | GAGGGCGCCC          | GCCGCCCTTC  | CGAGCCCGCC | GCCGCGCCC  | GGAGCCCGCA   |
| 180  | AGGACGAGCC | GAGGCCAAGA          | GGCCCAGAAG  | ACTCCGCTCT | GTGACGTTCA | CATGGTGAAG   |
| 240  | ACTGCAAGGA | GTCGCGGTGG          | CCCCGACGCC  | TCATCATCCC | GAGGAGGCGC | CGAGAGCGGC   |
| 300  | TGTGCTTTGG | TGTTGGTGCA          | AAGAGCCTGG  | TTGGCCAAAG | GTGGTACCAG | CCCAGATGAT   |
| 360  | AATATTTTGC | .TACTTGTACA         | AGGAGGAGCA. | GTGTTATTCT | ATGCTTGCAG | - ACTAGCATTT |
| 420  | ATGTCATCTT | ATCAAAGATG          | AATAAAGTAC  | ACTACTGTGG | GATGACGTGT | ACTTCAACCA   |
| 480  | AATTATAA   | ACAATTGAAG          | TCTCTACCAG  | CCCCAGCTGC | TCTGCAGATG | AAATGAGCCC   |
| 540  | TTGCAGATAG | GTCCCAGAGT          | CAGTGTGCCT  | TTGAATTTAT | GAAGAAGAAG | AATCTTTGAA   |
| 600  | TAGATCTTAA | ACAGCCTATT          | CAAGAAACTT  | ATGACTTTAA | AACATTGTTC | TGATCCTGCC   |
| 660  | CCAGAAACCT | GTTATGCCAC          | CACTTCCATT  | TCCCTCTGAA | TGCTATGTGA | CCTGGATAAG   |
| 720  | ATCTGATTCA | CCTCAGTCCT          | AACCTATTTG  | TCAAGGCTGG | CTTATTAACA | ACTGGAGTTA   |
| 780  | TCTTTATTTA | CACCTGGGTT          | AAACATTGAT  | ATCGCATTGA | GTTATTACTG | TGAGCACATG   |
| 840  | TTAAAGGTAT | AGAGAAACTA          | ACTGCAACGC  | AAACTTACAA | CATGACAAGG | TCGACTGTGT   |
| 900  | AATTTGCCGT | TTTGAAAACA          | AATTCGGCAT  | ATTGTTTCGC | GAAGCCAGCA | TCAGAAACGT   |
| 960  | ATTAATATCA | AT <u>T</u> GAGGAAA | GÄAAAACATT  | GAACAGTCAA | ATTTGTTCTT | GGAAACTTTA   |
| 1020 | CTTTCATGTA | TTTAAAGTCT          | AGTGATATTT  | CATTTTGTGC | CCACCCTTTA | CAGCATAACC   |
| 1080 | CCATTACCTT | TCAATTAAAA          | TCTCATTAAT  | TATCTTTTCA | AGGGCTTTAC | AGTAGCAAAC   |
| 1140 | TGTATGAAGT | AATTAGTAAC          | TTTATATTTG  | TGTGGTGTCT | TCTTTCGAAG | AAAATTTTTT   |

| CATAGATAAT | AGTACATGTC | ACCTTAGGTA | GTAGGAAGAA | TTACAATTTC | TTTAAATCAT | 1200 |
|------------|------------|------------|------------|------------|------------|------|
| TTATCTGGAT | TTTTATGTTT | TATTAGCATT | TTCAAGAAGA | CGGATTATCT | AGAGAATAAT | 1260 |
| CATATATATG | CATACGTAAA | AATGGACCAC | AGTGACTTAT | TTGTAGTTGT | TAGTTGCCCT | 1320 |
| GCTACCTAGT | TTGTTAGTGC | ATTTGAGCAC | ACATTTTAAT | TTTCCTCTAA | TTAAAATGTG | 1380 |
| CAGTATTTTC | AGTGTCAAAT | ATATTTAACT | ATTTAGAGAA | TGATTTCCAC | CTTTATGTTT | 1440 |
| TAATATCCTA | GGCATCTGCT | GTAATAATAT | TTTAGAAAAT | GTTTGGAATT | TAAGAAATAA | 1500 |
| CTTGTGTTAC | TAATTTGTAT | AACCCATATC | TGTGCAATGG | AATATAAATA | TCACAAAGTT | 1560 |
| GTTTAAAAAA | ААААААААА  | AAATTCCTGC | GGCCGC     |            |            | 1596 |

#### (2) INFORMATION FOR SEQ ID NO:20:

### (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 400 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

#### (ii) MOLECULE TYPE: None

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met Ala Trp Arg Arg Glu Ala Gly Val Gly Ala Arg Gly Val Leu 1 15 Ala Leu Ala Leu Leu Ala Leu Cys Val Pro Gly Ala Arg Gly 25 Arg Ala Leu Glu Trp Phe Ser Ala Val Val Asn Ile Glu Tyr Val Asp 35 40 Pro Gln Thr Asn Leu Thr Val Trp Ser Val Ser Glu Ser Gly Arg Phe 55 Gly Asp Ser Ser Pro Lys Glu Gly Ala His Gly Leu Val Gly Val Pro 75 80 Trp Ala Pro Gly Gly Asp Leu Glu Gly Cys Ala Pro Asp Thr Arg Phe 85 90 Phe Val Pro Glu Pro Gly Gly Arg Gly Ala Ala Pro Trp Val Ala Leu 105 Val Ala Arg Gly Gly Cys Thr Phe Lys Asp Lys Val Leu Val Ala Ala

|            |     | 115 |     |            |     |     | 120      |      |          |     |              | 125        |        |          |     |
|------------|-----|-----|-----|------------|-----|-----|----------|------|----------|-----|--------------|------------|--------|----------|-----|
| Arg        | Arg | Asn | Ala | Ser        | Ala | Val | Val      | Leu  | Tyr      | Asn | Glu          | Glu        | Arg    | Tyr      | Gly |
|            | 130 |     |     |            |     | 135 |          |      |          |     | 140          |            |        |          |     |
| Asn        | Ile | Thr | Leu | Pro        | Met | Ser | His      | Ala  | Gly      | Thr | Gly          | Asn        | Ile    | Val      | Val |
| 145        |     |     |     |            | 150 |     |          |      |          | 155 |              |            |        |          | 160 |
| Ile        | Met | Ile | Ser | Tyr        | Pro | ГÀв | Gly      | Arg  | Glu      | Ile | Leu          | Glu        | Leu    | Val      | Gln |
|            |     |     |     | 165        |     |     |          |      | 170      |     |              |            |        | 175      |     |
| Lys        | Gly | Ile | Pro | Val        | Thr | Met | Thr      | Ile  | Gly      | Val | Gly          | Thr        | Arg    | His      | Val |
|            |     |     | 180 |            |     |     |          | 185  |          |     |              |            | 190    |          |     |
| Gln        | Glu | Phe | Ile | Ser        | Gly | Gln | Ser      | Val  | Val      | Phe | Val          | Ala        | Ile    | Ala      | Phe |
|            |     | 195 |     |            |     |     | 200      |      |          |     |              | 205        |        |          |     |
| Ile        | Thr | Met | Met | Ile        | Ile | Ser | Leu      | Ala  | Trp      | Leu | Ile          | Phe        | Tyr    | Tyr      | Ile |
|            | 210 |     |     |            |     | 215 |          |      |          |     | 220          |            |        |          |     |
| Gln        | Arg | Phe | Leu | Tyr        | Thr | Gly | Ser      | Gln  | Ile      | Gly | Ser          | Gln        | Ser    | His      | Arg |
| 225        |     |     |     |            | 230 |     |          |      |          | 235 |              |            |        |          | 240 |
| Lys        | Glu | Thr | ГЛа | Lys        | Val | Ile | Gly      | Gln  | Leu      | Leu | Leu          | His        | Thr    | Val      | ГÀв |
|            |     |     |     | 245        |     |     |          |      | 250      |     |              |            |        | 255      |     |
| His        | Gly | Glu | Lys | Gly        | Ile | Asp | Val      | Asp  | Ala      | Glu | Asn          | Сув        |        | Val      | Сув |
|            |     |     | 260 |            |     |     |          | 265  |          |     |              |            | 270    |          |     |
| Ile        | Glu |     | Phe | Lys        | Val | ГÀв | _        | Ile  | Ile      | Arg | Ile          |            | Pro    | Сув      | Lys |
|            |     | 275 |     |            |     |     | 280      |      |          |     | _            | 285        |        |          |     |
| His        | Ile |     | His | Arg        |     |     |          | Asp  | Pro      | Trp |              | Leu        | Asp    | HIB      | Arg |
|            | 290 | •   |     |            |     | 295 |          |      |          | _   | 300          | _          |        | _        | _   |
|            | Сув | Pro | Met | Сув        |     | Leu | Asp      | Val  | IIe      |     | Ala          | Leu        | GIA    | Tyr      |     |
| 305        |     |     |     |            | 310 |     | -3       | 30.4 | <b>-</b> | 315 | <b>3</b>     | <b>a</b> 1 |        | <b>D</b> | 320 |
| GIA        | Glu | Pro | GIÀ | _          | Val | GIN | GIU      | wer  |          | Ala | Pro          | GIU        | Ser    |          | PFO |
| <b>~</b> 1 | •   | •   |     | 325        |     | 3   | <b>T</b> | 0    | 330      | 31- | T            | D===       | 7      | 335      | 7   |
| GIY        | Arg | Asp |     |            | Ala | ABN | Leu      | 345  | rea      | AIA | Leu          | Pro        | 350    | Asp      | ивр |
| <b>61</b>  | 0   | 2   | 340 |            | S   | D   | Dwa      |      | 21-      | 50= | Dwo          | 212        |        | 50=      | C1  |
| GIĀ        | Ser | _   | _   | ser        | ser | Pro | 360      |      | Ala      | ser | PIG          | 365        | GIU    | ser      | GIU |
| D-10       | a1- | 355 |     | D          |     | Dho |          |      | 3        | 210 | <b>61.</b> - |            | n en   | Th-      | 71- |
| PFO        | Gln | -   | мар | PIO        | ser | 375 |          | GIÀ  | wab      | uld | 38 <u>0</u>  |            | - nail | Inc      | wrq |
| T 0        | 370 |     | 71- | <b>a</b> 1 | N   |     |          | 80=  | n        | u:~ |              |            | Dro    | Tle      | Sor |
| 385        | Leu | GIU | wra | GIĀ        | 390 |     | ьвр      | ser  | arg      | 395 |              | GIY        | FLU    | 116      | 400 |
| 203        |     |     |     |            | 220 |     |          |      |          |     |              |            |        |          | 400 |

#### (2) INFORMATION FOR SEQ ID NO:21:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 291 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Met Asp Lys Gly Ser Ala Gly His Pro Gly Gly Val Leu Val Trp Gly 1 Arg Ser Pro Ala Pro Thr Ala Leu Trp Gly Ala Ser Pro Trp Leu Ser 25 Pro Leu Thr Ser Ala Leu Arg Gln Pro Leu His Arg Ala Pro Leu Leu 40 Pro Gly Gln Leu Cys Trp Ser Pro Arg Pro Leu Glu Lys Asn Lys Ala Met Gly Arg Pro Leu Leu Pro Leu Leu Leu Leu Cln Pro Pro 65 70 80 75 Ala Phe Leu Gln Pro Gly Gly Ser Thr Gly Ser Gly Pro Ser Tyr Leu 85 90 Tyr Gly Val Thr Gln Pro Lys His Leu Ser Ala Ser Met Gly Gly Ser 105 Val Glu Ile Pro Phe Ser Phe Tyr Tyr Pro Trp Glu Leu Ala Ile Val 115 120 125 Pro Asn Val Arg Ile Ser Trp Arg Arg Gly His Phe His Gly Gln Ser 135 Phe Tyr Ser Thr Arg Pro Pro Ser Ile His Lys Asp Tyr Val Asn Arg 145 150 155 160 Leu Phe Leu Asn Trp Thr Glu Gly Gln Glu Ser Gly Phe Leu Arg Ile 165 170 Ser Asn Leu Arg Lys Glu Asp Gln Ser Val Tyr Phe Cys Arg Val Glu 190 185

Leu Asp Thr Arg Arg Ser Gly Arg Gln Gln Leu Gln Ser Ile Lys Gly 195 Thr Lys Leu Thr Ile Thr Gln Ala Val Thr Thr Thr Thr Trp Arg 210 215 220 Pro Ser Ser Thr Thr The Ala Gly Leu Arg Val Thr Glu Ser Lys 230 235 Gly His Ser Glu Ser Trp His Leu Ser Leu Asp Thr Ala Ile Arg Val 250 245 Ala Leu Ala Val Ala Val Leu Lys Thr Val Ile Leu Gly Leu Leu Cys 260 265 270 Leu Leu Leu Trp Trp Arg Arg Lys Gly Ser Arg Ala Pro Ser 280 285 Ser Asp Phe 290

#### (2) INFORMATION FOR SEQ ID NO:22:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 293 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

 Met
 Thr
 Val
 Ser
 Gln
 Arg
 Phe
 Gln
 Leu
 Ser
 Asn
 Ser
 Gly
 Pro
 Asn
 Ser

 1
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 1
 10
 15
 15

 Thr
 Ile
 Lys
 Met
 Lys
 Ile
 Ala
 Leu
 Arg
 Val
 Leu
 His
 Leu
 Glu
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 Arg
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 Ile
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| 65  |     |     |     |     | 70  |     |     |     |      | 75  |     |     |     |     | 80  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Ser | Asp | Lys | Pro | Gly | Met | Glu | Glu  | Lys | Ala | Gln | Pro | Pro | Glu |
|     |     |     |     | 85  |     |     |     |     | 90   |     |     |     |     | 95  |     |
| Ala | Gly | Pro | Gln | Gly | Leu | His | Aap | Leu | Gly  | Arg | Ser | Ser | Ser | Ser | Leu |
|     |     |     | 100 |     |     |     |     | 105 |      |     |     |     | 110 |     |     |
| Leu | Ala | Ser | Pro | Gly | His | Ile | Ser | Val | Гув  | Glu | Pro | Thr | Pro | Ser | Ile |
|     |     | 115 |     |     |     |     | 120 |     |      |     |     | 125 |     |     | •   |
| Ala | Ser | Asp | Ile | Ser | Leu | Pro | Ile | Ala | Thr  | Gln | Glu | Leu | Arg | Gln | Arg |
|     | 130 |     |     |     |     | 135 |     |     |      |     | 140 |     |     |     |     |
| Leu | Arg | Gln | Leu | Glu | Asn | Gly | Thr | Thr | Leu  | Gly | Gln | Ser | Pro | Leu | Gly |
| 145 |     |     |     |     | 150 |     |     |     |      | 155 |     |     |     |     | 160 |
| Gln | Ile | Gln | Leu | Thr | Ile | Arg | His | Ser | Ser  | Gln | Arg | Asn | Lys | Leu | Ile |
|     |     |     |     | 165 |     |     |     |     | 170  |     |     |     |     | 175 |     |
| Val | Val | Val | His | Ala | Сув | Arg | Asn | Leu | Ile  | Ala | Phe | Ser | Glu | Asp | Gly |
|     |     |     | 180 |     |     |     |     | 185 |      |     |     |     | 190 |     |     |
| Ser | Aap | Pro | Tyr | Val | Arg | Met | Tyr | Leu | Leu  | Pro | Asp | Lys | Arg | Arg | Ser |
|     |     | 195 |     |     |     |     | 200 |     |      |     |     | 205 |     |     |     |
| Gly |     | Arg | Lys | Thr | His | Val | Ser | Lys | Lys  | Thr | Leu | Asn | Pro | Val | Phe |
|     | 210 |     |     |     | •   | 215 |     |     |      |     | 220 |     |     |     |     |
|     | Gln | Ser | Phe | Asp | Phe | Ser | Val | Ser | Leu  | Pro | Glu | Val | Gln | Arg | Arg |
| 225 |     |     |     |     | 230 |     |     |     |      | 235 |     |     |     |     | 240 |
| Thr | Leu | Asp | Val |     | Val | Lys | Asn | Ser | Gly  | Gly | Phe | Leu | Ser | Lys | Asp |
|     |     |     |     | 245 |     |     | -   | -   | 250· |     |     |     |     | 255 |     |
| Lys | Gly | Leu |     | Gly | Lys | Val | Leu |     | Ala  | Leu | Ala | Ser | Glu | Glu | Leu |
|     |     |     | 260 |     |     |     |     | 265 |      |     |     |     | 270 |     |     |
| Ala | Lys |     | Trp | Thr | Gln | Trp |     | Asp | Leu  | Thr | Glu |     | Gly | Thr | Arg |
|     |     | 275 |     |     |     |     | 280 |     |      |     |     | 285 |     |     |     |
| Pro | Gln | Ala | Met | Thr |     |     |     |     |      |     |     |     |     |     |     |
|     | 290 |     |     |     |     |     |     |     |      |     |     |     |     |     |     |

## (2) INFORMATION FOR SEQ ID NO:23:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 206 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single

#### (D) TOPOLOGY: linear

#### (ii) MOLECULE TYPE: None

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Met Glu Arg Arg His Pro Val Cys Ser Gly Thr Cys Gln Pro Thr Gln 1 5 Phe Arg Cys Ser Asn Gly Cys Cys Ile Asp Ser Phe Leu Glu Cys Asp 20 25 Asp Thr Pro Asn Cys Pro Asp Ala Ser Asp Glu Ala Ala Cys Glu Lys 45 40 Tyr Thr Ser Gly Phe Asp Glu Leu Gln Arg Ile His Phe Pro Ser Asp 60 55 Lys Gly His Cys Val Asp Leu Pro Asp Thr Gly Leu Cys Lys Glu Ser 70 75 Ile Pro Arg Trp Tyr Tyr Asn Pro Phe Ser Glu His Cys Ala Arg Phe 85 90 Thr Tyr Gly Gly Cys Tyr Gly Asn Lys Asn Asn Phe Glu Glu Glu Gln 105 Gln Cys Leu Glu Ser Cys Arg Gly Ile Ser Lys Lys Asp Val Phe Gly 115 120 125 Leu Arg Arg Glu Ile Pro Ile Pro Ser Thr Gly Ser Val Glu Met Ala 135 Val Ala Val Phe Leu Val Ile Cys Ile Val Val Val Ala Ile Leu 160 155 145 150 Gly Tyr Cys Phe Phe Lys Asn Gln Arg Lys Asp Phe His Gly His His 170 165 His His Pro Pro Pro Thr Pro Ala Ser Ser Thr Val Ser Thr Thr Glu 185 Asp Thr Glu His Leu Val Tyr Asn His Thr Thr Arg Pro Leu 195 200 205

#### (2) INFORMATION FOR SEQ ID NO:24:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 220 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met Ala Gly Leu Ser Arg Gly Ser Ala Arg Ala Leu Leu Ala Ala Leu 10 Leu Ala Ser Thr Leu Leu Ala Leu Leu Val Ser Pro Ala Arg Gly Arg 25 30 Gly Gly Arg Asp His Gly Asp Trp Asp Glu Ala Ser Arg Leu Pro Pro 40 Leu Pro Pro Arg Glu Asp Ala Ala Arg Val Ala Arg Phe Val Thr His Val Ser Asp Trp Gly Ala Leu Ala Thr Ile Ser Thr Leu Glu Ala Val 70 75 Arg Gly Arg Pro Phe Ala Asp Val Leu Ser Leu Ser Asp Gly Pro Pro 90 Gly Ala Gly Ser Gly Val Pro Tyr Phe Tyr Leu Ser Pro Leu Gln Leu 100 105 - -Ser Val Ser Asn Leu Gln Glu Asn Pro Tyr Ala Thr Leu Thr Met Thr Leu Ala Gln Thr Asn Phe Cys Lys Lys His Gly Phe Asp Pro Gln Ser 140 130 135 Pro Leu Cys Val His Ile Met Leu Ser Gly Thr Val Thr Lys Val Asn Glu Thr Glu Met Asp Ile Ala Lys His Ser Leu Phe Ile Arg His Pro 170 165 Glu Met Lys Thr Trp Pro Ser Ser His Asn Trp Phe Phe Ala Lys Leu 185 180 Asn Ile Thr Asn Ile Trp Val Leu Asp Tyr Phe Gly Gly Pro Lys Ile 205 Val Thr Pro Glu Glu Tyr Tyr Asn Val Thr Val Gln

210 215 220

#### (2) INFORMATION FOR SEQ ID NO:25:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 197 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Met Asp His His Cys Pro Trp Leu Asn Asn Cys Val Gly His Tyr Asn 1 5 10 His Arg Tyr Phe Phe Ser Phe Cys Phe Phe Met Thr Leu Gly Cys Val 20 25 Tyr Cys Ser Tyr Gly Ser Trp Asp Leu Phe Arg Glu Ala Tyr Ala Ala 40 Ile Glu Lys Met Lys Gln Leu Asp Lys Asn Lys Leu Gln Ala Val Ala 50 55 60 Asn Gln Thr Tyr His Gln Thr Pro Pro Pro Thr Phe Ser Phe Arg Glu 70 75 Arg Met Thr His Lys Ser Leu Val Tyr Leu Trp Phe Leu Cys Ser Ser 95 Val Ala Leu Ala Leu Gly Ala Leu Thr Val Trp His Ala Val Leu Ile 105 100 Ser Arg Gly Glu Thr Ser Ile Glu Arg His Ile Asn Lys Lys Glu Arg 120 Arg Arg Leu Gln Ala Lys Gly Arg Val Phe Arg Asn Pro Tyr Asn Tyr 130 135 Gly Cys Leu Asp Asn Trp Lys Val Phe Leu Gly Val Asp Thr Gly Arg 150 155 His Trp Leu Thr Arq Val Leu Leu Pro Ser Thr His Leu Pro His Gly 170 175 165

Asn Gly Met Ser Trp Glu Pro Pro Pro Trp Val Thr Ala His Ser Ala 180 185 190 Ser Val Met Ala Val

195

- (2) INFORMATION FOR SEQ ID NO:26:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 451 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Met Ala Pro Leu Gly Met Leu Leu Gly Leu Leu Met Ala Ala Cys Phe 10 Thr Phe Cys Leu Ser His Gln Asn Leu Lys Glu Phe Ala Leu Thr Asn 25 Pro Glu Lys Ser Ser Thr Lys Glu Thr Glu Arg Lys Glu Thr Lys Ala 45 35 Glu Glu Glu Leu Asp Ala Glu Val Leu Glu Val Phe His Pro Thr His 55 Glu Trp Gln Ala Leu Gln Pro Gly Gln Ala Val Pro Ala Gly Ser His 70 65 Val Arg Leu Asn Leu Gln Thr Gly Glu Arg Glu Ala Lys Leu Gln Tyr 90 Glu Asp Lys Phe Arg Asn Asn Leu Lys Gly Lys Arg Leu Asp Ile Asn 105

Thr Asn Thr Tyr Thr Ser Gln Asp Leu Lys Ser Ala Leu Ala Lys Phe
115 120 125

Lys Glu Gly Ala Glu Met Glu Ser Ser Lys Glu Asp Lys Ala Arg Gln

130 135 140

Ala Glu Val Lys Arg Leu Phe Arg Pro Ile Glu Glu Leu Lys Lys Asp

| 145 |     |     |     |     | 150 |      |     |     |     | 155 |     |     |     |     | 160 |
|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Asp | Glu | Leu | Asn | Val | Val. | Ile | Glu | Thr | qeA | Met | Gln | Ile | Met | Val |
|     |     |     |     | 165 |     |      |     |     | 170 |     |     |     |     | 175 |     |
| Arg | Leu | Ile | Asn | Lys | Phe | Asn  | Ser | Ser | Ser | Ser | Ser | Leu | Glu | Glu | Lys |
|     |     |     | 180 |     |     |      |     | 185 |     |     | •   |     | 190 |     |     |
| Ile | Ala | Ala | Leu | Phe | Авр | Leu  | Glu | Tyr | Tyr | Val | His | Gln | Met | Asp | Asn |
|     |     | 195 |     |     |     |      | 200 |     |     |     |     | 205 |     |     |     |
| Ala | Gln | Asp | Leu | Leu | Ser | Phe  | Gly | Gly | Leu | Gln | Val | Val | Ile | Asn | Gly |
|     | 210 |     |     |     |     | 215  |     |     |     |     | 220 |     |     |     |     |
| Leu | Asn | Ser | Thr | Glu | Pro | Leu  | Val | Lys | Glu | Tyr | Ala | Ala | Phe | Val | Leu |
| 225 |     |     |     |     | 230 |      |     |     |     | 235 |     |     |     |     | 240 |
| Gly | Ala | Ala | Phe | Ser | Ser | Asn  | Pro | Lys | Val | Gln | Val | Glu | Ala | Ile | Glu |
| •   |     |     |     | 245 |     |      |     |     | 250 |     |     |     |     | 255 |     |
| Gly | Gly | Ala | Leu | Gln | Lys | Leu  | Leu | Val | Ile | Leu | Ala | Thr | Glu | Gln | Pro |
|     |     |     | 260 |     |     |      |     | 265 |     |     |     |     | 270 |     |     |
| Leu | Thr | Ala | Lys | Lys | Lys | Val  | Leu | Phe | Ala | Leu | Сув | Ser | Leu | Leu | Arg |
|     |     | 275 |     |     |     |      | 280 |     |     | •   |     | 285 |     |     |     |
| His | Phe | Pro | Tyr | Ala | Gln | Arg  | Gln | Phe | Leu | Lys | Leu | Gly | Gly | Leu | Gln |
|     | 290 |     |     |     |     | 295  |     |     |     |     | 300 |     |     |     |     |
| Val | Leu | Arg | Thr | Leu | Val | Gln  | Glu | Lys | Gly | Thr | Glu | Val | Leu | Ala | Val |
| 305 |     |     |     |     | 310 |      |     |     |     | 315 |     |     |     |     | 320 |
| Arg | Val | Val | Thr | Leu | Leu | Tyr  | qaA | Leu | Val | Thr | Glu | Lys | Met | Phe | Ala |
|     |     |     |     | 325 |     |      |     |     | 330 |     |     |     |     | 335 |     |
| Glu | Glu | Glu | Ala | Glu | Leu | Thr  | Gln | Glu | Met | Ser | Pro | Glu | Lys | Leu | Gln |
|     |     |     | 340 |     |     |      |     | 345 |     |     |     |     | 350 |     |     |
| Gln | Tyr | Arg | Gln | Val | His | Leu  | Leu | Pro | Gly | Leu | Trp | Glu | Gln | Gly | Trp |
|     |     | 355 |     |     |     |      | 360 |     |     |     |     | 365 |     |     |     |
| Сув | Glu | Ile | Thr | Ala | His | Leu  | Leu | Ala | Leu | Pro | Glu | His | Asp | Ala | Arg |
|     | 370 |     |     |     |     | 375  |     |     |     |     | 380 |     |     |     |     |
| Glu | Lys | Val | Leu | Gln | Thr | Leu  | Gly | Val | Leu | Leu | Thr | Thr | Cys | Arg | Asp |
| 385 |     |     |     |     | 390 |      |     |     | •   | 395 |     |     |     |     | 400 |
| Arg | Tyr | Arg | Gln | Asp | Pro | Gln  | Leu | Gly | Arg | Thr | Leu | Ala | Ser | Leu | Gln |
| _   | -   | _   |     | 405 |     |      |     |     | 410 |     |     |     |     | 415 |     |
| Ala | Glu | Tyr | Gln | Val | Leu | Ala  | Ser | Leu | Glu | Leu | Gln | Asp | Gly | Glu | Asp |
|     |     | -   | 420 |     |     |      |     | 425 |     |     |     |     | 430 |     |     |
| Glu | Gly | Tyr | Phe | Gln | Glu | Leu  | Leu | Glv | Ser | Val | Asn | Ser | Leu | Leu | Lys |

435 440 445

Glu Leu Arg 450

#### (2) INFORMATION FOR SEQ ID NO:27:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 254 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

135

150

Met Trp Gln Ala Gly Lys Arg Gln Ala Ser Arg Ala Phe Ser Leu Tyr 1 10 15 Ala Asn Ile Asp Ile Leu Arg Pro Tyr Phe Asp Val Glu Pro Ala Gln 25 Val Arg Ser Arg Leu Leu Glu Ser Met Ile Pro Ile Lys Met Val Asn 40 Phe Pro Gln Lys Ile Ala Gly Glu Leu Tyr Gly Pro Leu Met Leu Val 55 Phe Thr Leu Val Ala Ile Leu Leu His Gly Met Lys Thr Ser Asp Thr 70 75 Ile Ile Arg Glu Gly Thr Leu Met Gly Thr Ala Ile Gly Thr Cys Phe 85 90 Gly Tyr Trp Leu Gly Val Ser Ser Phe Ile Tyr Phe Leu Ala Tyr Leu 100 105 Cys Asn Ala Gln Ile Thr Met Leu Gln Met Leu Ala Leu Leu Gly Tyr 115 120 Gly Leu Phe Gly His Cys Ile Val Leu Phe Ile Thr Tyr Asn Ile His

Leu His Ala Leu Phe Tyr Leu Phe Trp Leu Leu Val Gly Gly Leu Ser

140

160

155

145

Thr Leu Arg Met Val Ala Val Leu Val Ser Arg Thr Val Gly Pro Thr 165 Gln Arg Leu Leu Cys Gly Thr Leu Ala Ala Leu His Met Leu Phe 180 185 Leu Leu Tyr Leu His Phe Ala Tyr His Lys Val Val Glu Gly Ile Leu 200 Asp Thr Leu Glu Gly Pro Asn Ile Pro Pro Ile Gln Arg Val Pro Arg 215 210 220 Asp Ile Pro Ala Met Leu Pro Ala Ala Arg Leu Pro Thr Thr Val Leu 225 230 235 240 Asn Ala Thr Ala Lys Ala Val Ala Val Thr Leu Gln Ser His 250 245

#### (2) INFORMATION FOR SEQ ID NO:28:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 221 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

 Met
 Gly
 Ser
 Glu
 Asn
 Glu
 Ala
 Leu
 Asp
 Leu
 Ser
 Met
 Lys
 Ser
 Val
 Fro

 Trp
 Leu
 Lys
 Ala
 Gly
 Glu
 Val
 Ser
 Pro
 Pro
 Pro
 Pro
 Glu
 Pro
 Glu
 Asp
 Glu
 Asp
 Ala
 Ala
 Ala
 Ala
 Ala
 Ala
 Ala
 Arg
 Lys
 Ser
 Glu
 Pro
 Pro

85 90 95 Asp Ala Ala Thr Glu Met Leu Ser Gln Pro Asn His Pro Ser Gly Glu 100 105 Val Lys Ala Glu Asn Asn Ile Glu Met Val Gly Glu Ser Gln Ala Ala 115 120 125 Lys Val Ile Val Ser Val Glu Asp Ala Val Pro Thr Ile Phe Cys Gly 135 Lys Ile Lys Gly Leu Ser Gly Val Ser Thr Lys Asn Phe Ser Phe Lys 145 150 155 160 Arg Glu Asp Ser Val Leu Gln Gly Tyr Asp Ile Asn Ser Gln Gly Glu 165 170 Glu Ser Met Gly Asn Ala Glu Pro Leu Arg Lys Pro Ile Lys Asn Arg 180 185 190 Ser Ile Lys Leu Lys Lys Val Asn Ser Gln Glu Val His Met Leu Pro 200 Ile Lys Lys Gln Arg Leu Ala Thr Phe Phe Pro Arg Lys 215 220

#### (2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 266 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

 Met
 Val
 Lys
 Val
 Thr
 Phe
 Asn
 Ser
 Ala
 Leu
 Ala
 Gln
 Lys
 Glu
 Ala
 Lys

 Lys
 5
 5
 5
 10
 5
 15
 15

 Lys
 Asp
 Glu
 Glu
 Ala
 Leu
 Ile
 Ile
 Pro
 Pro
 Asp

 Ala
 Val
 Ala
 Val
 Asp
 Cys
 Lys
 Asp
 Pro
 Asp
 Val
 Val
 Pro
 Val
 Gly

 Ala
 Val
 Ala
 Val
 Asp
 Cys
 Lys
 Asp
 Pro
 Asp
 Val
 Val
 Pro
 Val
 Gly

 Ala
 Val
 Asp
 Cys
 Lys
 Asp
 Pro
 Asp
 Val
 Val
 Pro
 Val
 Gly

| Gln | Arg | Arg | Ala | Trp | Сув | Trp | Сув | Met | Сув | Phe | GIÀ | Leu | Ala | Pne | Met |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     | 50  |     |     |     | •   | 55  |     |     |     |     | 60  |     |     |     |     |
| Leu | Ala | Gly | Val | Ile | Leu | Gly | Gly | Ala | Tyr | Leu | Tyr | Lys | Tyr | Phe | Ala |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Leu | Gln | Pro | Asp | Asp | Val | Tyr | Tyr | Сув | Gly | Ile | Lys | Tyr | Ile | ГЛВ | Авр |
|     | ٠   |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| qaA | Val | Ile | Leu | Asn | Glu | Pro | Ser | Ala | Asp | Ala | Pro | Ala | Ala | Leu | Tyr |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Gln | Thr | Ile | Glu | Glu | Asn | Ile | Lys | Ile | Phe | Glu | Glu | Glu | Glu | Val | Glu |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Phe | Ile | Ser | Val | Pro | Val | Pro | Glu | Phe | Ala | Asp | Ser | Asp | Pro | Ala | Asn |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 | ·   |     |     |     |
| Ile | Val | His | Asp | Phe | Asn | ГÀв | Lys | Leu | Thr | Ala | Tyr | Leu | Asp | Leu | Asn |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Leu | Asp | ГÀв | Сув | Tyr | Val | Ile | Pro | Leu | Asn | Thr | Ser | Ile | Val | Met | Pro |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Pro | Arg | Asn | Leu | Leu | Glu | Leu | Leu | Ile | Asn | Ile | ГÀв | Ala | Gly | Thr | Tyr |
|     |     |     | 180 |     |     |     |     | 185 | •   |     |     |     | 190 |     |     |
| Leu | Pro | Gln | Ser | Tyr | Leu | Ile | His | Glu | His | Met | Val | Ile | Thr | Asp | Arg |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Ile | Glu | Asn | Ile | Asp | His | Leu | Gly | Phe | Phe | Ile | Tyr | Arg | Leu | Сла | His |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Asp | Lys | Glu | Thr | Tyr | Lys | Leu | Gln | Arg | Arg | Glu | Thr | Ile | Lys | Gly | Ile |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 | •   |     |     |     | 240 |
| Gln | Lys | Arg | Glu | Ala | Ser | Asn | Сув | Phe | Ala | Ile | Arg | His | Phe | Glu | Asn |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Lys | Phe | Ala | Val | Glu | Thr | Leu | Ile | Сув | Ser |     |     |     |     |     |     |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     |     |     |     |

## (2) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 251 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: None

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

| Met | Pro | Thr | Gly | Asp | Phe | Asp | Ser | Lys  | Pro | Ser | Trp | Ala | Asp | Gln | Val |
|-----|-----|-----|-----|-----|-----|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|
| 1   |     |     |     | 5   |     | ·   |     |      | 10  |     |     |     |     | 15  |     |
| Glu | Glu | Glu | Gly | Glu | Asp | Asp | Lys | Сув  | Val | Thr | Ser | Glu | Leu | Leu | Lys |
|     |     |     | 20  |     |     |     |     | 25   |     |     |     |     | 30  |     |     |
| Gly | Ile | Pro | Leu | Ala | Thr | Gly | Asp | Thr  | Ser | Pro | Glu | Pro | Glu | Leu | Leu |
|     |     | 35  |     |     |     |     | 40  |      |     |     |     | 45  |     | •   |     |
| Pro | Gly | Ala | Pro | Leu | Pro | Pro | Pro | Lys  | Glu | Val | Ile | Asn | Gly | Asn | Ile |
|     | 50  |     |     |     |     | 55  |     |      |     |     | 60  |     |     |     |     |
| Lys | Thr | Val | Thr | Glu | Tyr | ГÀв | Ile | Asp  | Glu | Asp | Gly | Lys | Lys | Phe | Lys |
| 65  |     |     |     |     | 70  |     |     |      |     | 75  |     |     |     |     | 80  |
| Ile | Val | Arg | Thr | Phe | Arg | Ile | Glu | Thr  | Arg | Lys | Ala | Ser | Lys | Ala | Val |
|     |     |     |     | 85  |     |     |     |      | 90  |     |     |     |     | 95  |     |
| Ala | Arg | Arg | Lys | Asn | Trp | Lys | ГÀв | Phe  | Gly | Asn | Ser | Glu | Phe | Asp | Pro |
|     |     |     | 100 |     |     |     |     | 105  |     |     |     |     | 110 |     |     |
| Pro | Gly | Pro | Asn | Val | Ala | Thr | Thr | Thr  | Val | Ser | Asp | Asp | Val | Ser | Met |
|     |     | 115 |     |     |     |     | 120 |      |     |     |     | 125 |     |     |     |
| Thr | Phe | Ile | Thr | Ser | Lys | Glu | Asp | Leu  | Asn | Сув | Gln | Glu | Glu | Glu | Asp |
|     | 130 |     |     |     |     | 135 |     |      |     |     | 140 |     |     |     |     |
| Pro | Met | Asn | Lys | Phe | Lys | Gly | Gln | Lys. | Ile | Val | Ser | Сув | Arg | Ile | Сув |
| 145 |     |     |     |     | 150 |     |     |      |     | 155 |     |     |     |     | 160 |
| Lys | Gly | Asp | His | Trp | Thr | Thr | Arg | Сув  | Pro | Tyr | Lys | Asp | Thr | Leu | Gly |
|     |     |     |     | 165 |     |     |     |      | 170 |     |     |     |     | 175 |     |
| Pro | Met | Gln | Lys | Glu | Leu | Ala | Glu | Gln  | Leu | Gly | Leu | Ser | Thr | Gly | Glu |
|     |     |     | 180 |     |     |     |     | 185  |     |     |     |     | 190 |     |     |
| Lys | Glu | Lys | Leu | Pro | Gly | Glu | Leu | Glu  | Pro | Val | Gln | Ala | Thr | Gln | Asn |
|     |     | 195 |     |     |     |     | 200 |      |     |     |     | 205 |     |     |     |
| Lys | Thr | Gly | Lys | Tyr | Val | Pro | Pro | Ser  | Leu | Arg | Asp | Gly | Ala | Ser | Arg |
|     | 210 |     |     |     |     | 215 |     |      |     |     | 220 |     |     |     |     |
| Arg | Gly | Glu | Ser | Met | Gln | Pro | Asn | Arg  | Arg | Ala | Asp | Asp | Asn | Ala | Thr |
| 225 |     |     |     |     | 230 |     |     |      |     | 235 |     |     |     |     | 240 |
| Ile | Arg | Val | Thr | Asn | Leu | Arg | Arg | Gly  | His | Ala |     |     |     |     |     |
|     |     |     |     | 245 |     |     |     |      | 250 |     |     |     |     |     |     |

#### (2) INFORMATION FOR SEQ ID NO:31:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 377 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Met Arg Arg Leu Asn Arg Lys Lys Thr Leu Ser Leu Val Lys Glu Leu 10 Asp Ala Phe Pro Lys Val Pro Glu Ser Tyr Val Glu Thr Ser Ala Ser 25 Gly Gly Thr Val Ser Leu Ile Ala Phe Thr Thr Met Ala Leu Leu Thr 35 40 Ile Met Glu Phe Ser Val Tyr Gln Asp Thr Trp Met Lys Tyr Glu Tyr 55 60 Glu Val Asp Lys Asp Phe Ser Ser Lys Leu Arg Ile Asn Ile Asp Ile 80 65 Thr Val Ala Met Lys Cys Gln Tyr Val Gly Ala Asp Val Leu Asp Leu 90 Ala Glu Thr Met Val Ala Ser Ala Asp Gly Leu Val Tyr Glu Pro Thr 100 105 Val Phe Asp Leu Ser Pro Gln Gln Lys Glu Trp Gln Arg Met Leu Gln 120 Leu Ile Gln Ser Arg Leu Gln Glu Glu His Ser Leu Gln Asp Val Ile 140 135 Phe Lys Ser Ala Phe Lys Ser Thr Ser Thr Ala Leu Pro Pro Arg Glu 145 160 150 Asp Asp Ser Ser Gln Ser Pro Asn Ala Cys Arg Ile His Gly His Leu 165 170 Tyr Val Asn Lys Val Ala Gly Asn Phe His Ile Thr Val Gly Lys Ala 185 190 180

| Ile | Pro | His | Pro | Arg | Gly | His | Ala | His | Leu | Ala | Ala | Leu | Val | Asn | His |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     | 195 |     |     | :   |     | 200 |     |     |     |     | 205 |     |     | •   |
| Glu | Ser | Tyr | Asn | Phe | Ser | His | Arg | Ile | Asp | His | Leu | ser | Phe | Gly | Glu |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Leu | Val | Pro | Ala | Ile | Ile | Asn | Pro | Leu | qaA | Gly | Thr | Glu | ГÀв | Ile | Ala |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Ile | Asp | His | Asn | Gln | Met | Phe | Gln | Tyr | Phe | Ile | Thr | Val | Val | Pro | Thr |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Lys | Leu | His | Thr | Tyr | Lув | Ile | Ser | Ala | Asp | Thr | His | Gln | Phe | Ser | Val |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Thr | Glu | Arg | Glu | Arg | Ile | Ile | Asn | His | Ala | Ala | Gly | Ser | His | Gly | Val |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Ser | Gly | Ile | Phe | Met | Lys | Tyr | Asp | Leu | Ser | Ser | Leu | Met | Val | Thr | Val |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| Thr | Glu | Glu | His | Met | Pro | Phe | Trp | Gln | Phe | Phe | Val | Arg | Leu | Сув | Gly |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Ile | Val | Gly | Gly | Ile | Phe | Ser | Thr | Thr | Gly | Met | Leu | His | Gly | Ile | Gly |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Lys | Phe | Ile | Val | Glu | Ile | Ile | Cys | Сув | Arg | Phe | Arg | Leu | Gly | Ser | Tyr |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| Lys | Pro | Val | Asn | Ser | Val | Pro | Phe | Glu | Asp | Gly | His | Thr | Asp | Asn | His |
|     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
| Leu | Pro | Leu | Leu | Glu | Asn | Asn | Thr | His |     |     |     |     |     |     |     |
|     | 370 |     |     |     |     | 375 |     |     |     |     |     |     |     |     |     |

- (2) INFORMATION FOR SEQ ID NO:32:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 250 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

| Met | GIY | ser | GII | ura | ser | Ala | AIA | AIG | Arg | PFO | ser | ser | Cys | Arg | MEG |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Lys | Gln | Glu | Asp | Asp | Arg | Asp | Gly | Leu | Leu | Ala | Glu | Arg | Glu | Gln | Glu |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  | •   |     |
| Glu | Ala | Ile | Ala | Gln | Phe | Pro | Tyr | Val | Glu | Phe | Thr | Gly | Arg | Авр | Ser |
|     |     | 35  |     |     |     |     | 40  |     | •   |     |     | 45  |     |     |     |
| Ile | Thr | Сув | Leu | Thr | Сув | Gln | Gly | Thr | Gly | Tyr | Ile | Pro | Thr | Glu | Gln |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Val | Asn | Glu | Leu | Val | Ala | Leu | Ile | Pro | His | Ser | Asp | Gln | Arg | Leu | Arg |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Pro | Gln | Arg | Thr | Lys | Gln | Tyr | Val | Leu | Leu | Ser | Ile | Leu | Leu | Сув | Leu |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Leu | Ala | Ser | Gly | Leu | Val | Val | Phe | Phe | Leu | Phe | Pro | His | Ser | Val | Leu |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     | ٠   |
| Val | Asp | Asp | Asp | Gly | Ile | Lys | Val | Val | Lys | Val | Thr | Phe | Asn | Lys | Gln |
|     |     | 115 |     | •   |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Asp | Ser | Leu | Val | Ile | Leu | Thr | Ile | Met | Ala | Thr | Leu | Lys | Ile | Arg | Asn |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Ser | Asn | Phe | Tyr | Thr | Val | Ala | Val | Thr | Ser | Leu | Ser | Ser | Gln | Ile | Gln |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     | •   |     |     | 160 |
| Tyr | Met | Asn | Thr | Val | Val | Ser | Thr | Tyr | Val | Thr | Thr | Asn | Val | Ser | Leu |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ile | Pro | Pro | Arg | Ser | Glu | Gln | Leu | Val | Asn | Phe | Thr | Gly | Lys | Alạ | Glu |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Met | Gly | _   | Pro | Phe | Ser | Tyr |     | Tyr | Phe | Phe | Сув |     | Val | Pro | Glu |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Ile | Leu | Val | His | Asn | Ile | Val | Ile | Phe | Met | Arg | Thr | Ser | Val | Lys | Ile |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Ser | Tyr | Ile | Gly | Leu | Met | Thr | Gln | Ser | Ser | Leu | Glu | Thr | His | His | Tyr |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Val | Asp | Сув | Gly | Gly | Asn | Ser | Thr | Ala | Ile |     |     |     |     |     |     |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     |     |     |

# (2) INFORMATION FOR SEQ ID NO:33:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 374 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Met Val Thr Cys Phe His Val Pro Tyr Ser Ala Leu Thr Met Phe Ile Ser Thr Glu Gln Thr Glu Arg Asp Ser Ala Thr Ala Tyr Arg Met Thr 20 25 30 Val Glu Val Leu Gly Thr Val Leu Gly Thr Ala Ile Gln Gly Gln Ile 40 Val Gly Gln Ala Asp Thr Pro Cys Phe Gln Asp Leu Asn Ser Ser Thr 55 60 Val Ala Ser Gln Ser Ala Asn His Thr His Gly Thr Thr Ser His Arg 70 75 Glu Thr Gln Lys Ala Tyr Leu Leu Ala Ala Gly Val Ile Val Cys Ile 90 Tyr Ile Ile Cys Ala Val Ile Leu Ile Leu Gly Val Arg Glu Gln Arg 100 105 110 Glu Pro Tyr Glu Ala Gln Gln Ser Glu Pro Ile Ala Tyr Phe Arg Gly 120 Leu Arg Leu Val Met Ser His Gly Pro Tyr Ile Lys Leu Ile Thr Gly 130 135 140 Phe Leu Phe Thr Ser Leu Ala Phe Met Leu Val Glu Gly Asn Phe Val 150 155 Leu Phe Cys Thr Tyr Thr Leu Gly Phe Arg Asn Glu Phe Gln Asn Leu 170 Leu Leu Ala Ile Met Leu Ser Ala Thr Leu Thr Ile Pro Ile Trp Gln 185 180 Trp Phe Leu Thr Arg Phe Gly Lys Lys Thr Ala Val Tyr Val Gly Ile 200 Ser Ser Ala Val Pro Phe Leu Ile Leu Val Ala Leu Met Glu Ser Asn

220 210 215 Leu Ile Ile Thr Tyr Ala Val Ala Val Ala Ala Gly Ile Ser Val Ala 230 235 225 Ala Ala Phe Leu Leu Pro Trp Ser Met Leu Pro Asp Val Ile Asp Asp 245 250 Phe His Leu Lys Gln Pro His Phe His Gly Thr Glu Pro Ile Phe Phe 260 265 Ser Phe Tyr Val Phe Phe Thr Lys Phe Ala Ser Gly Val Ser Leu Gly 275 280 Ile Ser Thr Leu Ser Leu Asp Phe Ala Gly Tyr Gln Thr Arg Gly Cys 295 300 Ser Gln Pro Glu Arg Val Lys Phe Thr Leu Asn Met Leu Val Thr Met 305 310 315 320 Ala Pro Ile Val Leu Ile Leu Leu Gly Leu Leu Phe Lys Met Tyr 330 325 Pro Ile Asp Glu Glu Arg Arg Gln Asn Lys Lys Ala Leu Gln Ala 350 340 345 Leu Arg Asp Glu Ala Ser Ser Ser Gly Cys Ser Glu Thr Asp Ser Thr 355 360 365 Glu Leu Ala Ser Ile Leu 370

- . (2) INFORMATION FOR SEQ ID NO:34:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 334 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Met Val Asn Asp Pro Pro Val Pro Ala Leu Leu Trp Ala Gln Glu Val 1 5 10 15

| G | ly  | Gln | Val | Leu | Ala | Gly | Arg | Ala | Arg | Arg | Leu | Leu | Leu | Gln | Phe           | Gly |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------------|-----|
|   |     |     |     | 20  | •   | •   |     |     | 25  |     |     |     |     | 30  |               |     |
| V | al  | Leu | Phe | Сув | Thr | Ile | Leu | Leu | Leu | Leu | Trp | Val | Ser | Val | Phe           | Leu |
|   |     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |               |     |
| T | yr  | Gly | Ser | Phe | Tyr | Tyr | Ser | Tyr | Met | Pro | Thr | Val | Ser | His | Leu           | Ser |
|   |     | 50  |     |     |     |     | 55  |     | •   |     |     | 60  |     |     |               |     |
| P | ro  | Val | His | Phe | Tyr | Tyr | Arg | Thr | Asp | Сув | Asp | Ser | Ser | Thr | Thr           | Ser |
| 6 | 5   |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |               | 80  |
| L | eu  | Сув | Ser | Phe | Pro | Val | Ala | Asn | Val | Ser | Leu | Thr | Lув | Gly | Gly           | Arg |
|   |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95            |     |
| A | sp  | Arg | Val | Leu | Met | Tyr | Gly | Gln | Pro | Tyr | Arg | Val | Thr | Leu | Glu           | Leu |
|   |     |     |     | 100 |     |     |     |     | 105 |     |     |     | •   | 110 |               |     |
| G | lu  | Leu | Pro | Glu | Ser | Pro | Val | Asn | Gln | yab | Leu | Gly | Met | Phe | Leu           | Val |
|   |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |               |     |
| T | hr  | Ile | Ser | Cys | Tyr | Thr | Arg | Gly | Gly | Arg | Ile | Ile | Ser | Thr | Ser           | Ser |
|   |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |               |     |
| A | rg  | Ser | Val | Met | Leu | His | Tyr | Arg | Ser | Asp | Leu | Leu | Gln | Met | Leu           | Aap |
| 1 | 45  |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |               | 160 |
| T | hr  | Leu | Val | Phe | Ser | Ser | Leu | Leu | Leu | Phe | Gly | Phe | Ala | Glu | Gln           | ГÀв |
|   |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175           |     |
| G | ln  | Leu | Leu | Glu | Val | Glu | Leu | Tyr | Ala | Asp | Tyr | Arg | Glu | Asn | Ser           | Tyr |
|   |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |               |     |
| V | al  | Pro | Thr | Thr | Gly | Ala | Ile | Ile | Glu | Ile | His | Ser | Lys | Arg | Ile           | Gln |
|   |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |               |     |
| I | eu  | Tyr | Gly | Ala | Tyr | Leu | Arg | Ile | His | Ala | His | Phe | Thr | Gly | Leu           | Arg |
|   |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |               |     |
| 1 | yr  | Leu | Leu | Tyr | Asn | Phe | Pro | Met | Thr | САв |     |     | Ile | Gly | Val           |     |
| 2 | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |               | 240 |
| S | Ser | Asn | Phe | Thr | Phe | Leu | Ser | Val | Ile | Val | Leu | Phe | Ser | Tyr | Met           | Gln |
|   |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | . <b>25</b> 5 |     |
| 2 | rp  | Val | Trp | Gly | Gly | Ile | Trp | Pro | Arg | His | Arg | Phe | ser | Leu | Gln           | Val |
|   |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |               |     |
| Į | yan | Ile | Arg | Lys | Arg | Asp | Asn | Ser | Arg | Lys | Glu | Val | Gln | Arg | Arg           | Ile |
|   |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |               |     |
| 5 | Ser | Ala | His | ln  | Pro | Gly | Pro | Glu | Gly | Gln | Glu | Glu | Ser | Thr | Pro           | Gln |
|   |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |               |     |

Ser Asp Val Thr Glu Asp Gly Glu Ser Pro Glu Asp Pro Ser Gly Thr

305 310 315 320

Glu Val Ser Cys Pro Arg Arg Arg Asn Gln Ile Ser Ser Pro

325 330

#### (2) INFORMATION FOR SEQ ID NO:35:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 276 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Met Thr His Pro Gly Thr Gly Asp Ile Ile Ala Val Met Ile Thr Glu Leu Arg Gly Lys Asp Ile Leu Ser Tyr Leu Glu Lys Asn Ile Ser Val 20 25 Gln Met Thr Ile Ala Val Gly Thr Arg Met Pro Pro Lys Asn Phe Ser 35 45 40 Arg Gly Ser Leu Val Phe Val Ser Ile Ser Phe Ile Val Leu Met Ile 55 60 Ile Ser Ser Ala Trp Leu Ile Phe Tyr Phe Ile Gln Lys Ile Arg Tyr 65 70 75 Thr Asn Ala Arg Asp Arg Asn Gln Arg Arg Leu Gly Asp Ala Ala Lys 85 90 Lys Ala Ile Ser Lys Leu Thr Thr Arg Thr Val Lys Lys Gly Asp Lys 100 105 110 Glu Thr Asp Pro Asp Phe Asp His Cys Ala Val Cys Ile Glu Ser Tyr 120 Lys Gln Asn Asp Val Val Arg Ile Leu Pro Cys Lys His Val Phe His 130 135 140 Lys Ser Cys Val Asp Pro Trp Leu Ser Glu His Cys Thr Cys Pro Met

155 160 150 145 Cys Lys Leu Asn Ile Leu Lys Ala Leu Gly Ile Val Pro Asn Leu Pro 170 175 Cys Thr Asp Asn Val Ala Phe Asp Met Glu Arg Leu Thr Arg Thr Gln 180 185 Ala Val Asn Arg Arg Ser Ala Leu Gly Asp Leu Ala Gly Asp Asn Ser 200 Leu Gly Leu Glu Pro Leu Arg Thr Ser Gly Ile Ser Pro Leu Pro Gln 220 210 215 Asp Gly Glu Leu Thr Pro Arg Thr Gly Glu Ile Asn Ile Ala Val Thr 235 230 Lys Glu Trp Phe Ile Ile Ala Ser Phe Gly Leu Leu Ser Ala Leu Thr 245 250 Leu Cys Tyr Met Ile Ile Arg Ala Thr Ala Ser Leu Asn Ala Asn Glu 260 265 270 Val Glu Trp Phe 275

- (2) INFORMATION FOR SEQ ID NO:36:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 210 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

 Met
 Ala
 Asn
 Ser
 Gly
 Leu
 Gln
 Leu
 Gly
 Phe
 Ser
 Met
 Ala
 Leu
 Leu

 1
 5
 10
 10
 15
 15

 Gly
 Trp
 Val
 Ala
 Cys
 Thr
 Ala
 Ile
 Pro
 Gln
 Trp
 Gln
 Met

 Ser
 Ser
 Tyr
 Ala
 Gly
 Asp
 Asn
 Ile
 Ile
 Thr
 Ala
 Gln
 Ala
 Met
 Tyr
 Lys

 35
 40
 40
 45
 45
 45

Gly Leu Trp Met Asp Cys Val Thr Gln Ser Thr Gly Met Met Ser Cys 50 55 60 Lys Met Tyr Asp Ser Val Leu Ala Leu Ser Ala Ala Leu Gln Ala Thr 75 70 Arg Ala Leu Met Val Val Ser Leu Val Leu Gly Phe Leu Ala Met Phe 85 90 Val Ala Thr Met Gly Met Lys Cys Thr Arg Cys Gly Gly Asp Asp Lys 100 105 Val Lys Lys Ala Arg Ile Ala Met Gly Gly Ile Ile Phe Ile Val 120 Ala Gly Leu Ala Ala Leu Val Ala Cys Ser Trp Tyr Gly His Gln Ile 130 135 140 Val Thr Asp Phe Tyr Asn Pro Leu Ile Pro Thr Asn Ile Lys Tyr Glu 150 155 Phe Gly Pro Ala Ile Phe Ile Gly Trp Ala Gly Ser Ala Leu Val Ile 165 170 Leu Gly Gly Ala Leu Leu Ser Cys Ser Cys Pro Gly Asn Glu Ser Lys 180 185 Ala Gly Tyr Arg Ala Pro Arg Ser Tyr Pro Lys Ser Asn Ser Ser Lys 200 205 Glu Tyr 210

- (2) INFORMATION FOR SEQ ID NO:37:
- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 476 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Met Ile Arg Pro Gln Leu Arg Thr Ala Gly Leu Gly Arg Cys Leu Leu

| 1   |           |            |       | 5         |       |          |            |      | 10      |             |          |     |       | 15         |              |
|-----|-----------|------------|-------|-----------|-------|----------|------------|------|---------|-------------|----------|-----|-------|------------|--------------|
| Pro | Gly       | Leu        | Leu   | Leu       | Leu   | Leu      | Val        | Pro  | Val     | Leu         | Trp      | Ala | Gly   | Ala        | Glu          |
|     |           |            | 20    |           |       |          |            | 25   |         |             |          |     | 30    |            |              |
| Lys | Leu       | His        | Thr   | Gln       | Pro   | Ser      | Cys        | Pro  | Ala     | Val         | Сув      | Gln | Pro   | Thr        | Arg          |
|     |           | 35         |       |           |       |          | 40         |      |         |             |          | 45  |       |            | •            |
| Cys | Pro       | Ala        | Leu   | Pro       | Thr   | Сув      | Ala        | Leu  | Gly     | Thr         | Thr      | Pro | Val   | Phe        | Asp          |
|     | 50        |            |       |           |       | 55       |            |      |         |             | 60       |     |       |            |              |
| Leu | Cys       | Arg        | Сув   | Сув       | Arg   | Val      | Сув        | Pro  | Ala     | Ala         | Glu      | Arg | Glu   | Val        | Сув          |
| 65  |           |            |       |           | 70    |          |            |      |         | 75          |          |     |       |            | 80           |
| Gly | Gly       | Ala        | Gln   | Gly       | Gln   | Pro      | Сув        | Ala  | Pro     | Gly         | Leu      | Gln | Cys   | Leu        | Gln          |
|     |           |            |       | 85        |       |          |            |      | 90      |             |          |     |       | 95         |              |
| Pro | Leu       | Arg        | Pro   | Gly       | Phe   | Pro      | Ser        | Thr  | Сув     | Gly         | Сув      | Pro | Thr   | Leu        | Gly          |
|     |           |            | 100   |           |       |          |            | 105  |         |             |          |     | 110   |            |              |
| Gly | Ala       | Val        | Сув   | Gly       | Ser   | Asp      | Arg        | Arg  | Thr     | Tyr         | Pro      | Ser | Met   | Сув        | Ala          |
|     |           | 115        |       |           |       |          | 120        |      |         |             |          | 125 |       |            |              |
| Leu | Arg       | Ala        | Glu   | Asn       | Arg   | Ala      | Ala        | Arg  | Arg     | Leu         | Gly      | Lys | Val   | Pro        | Ala          |
|     | 130       |            |       |           |       | 135      |            |      |         |             | 140      |     |       |            |              |
| Val | Pro       | Val        | Gln   | Trp       | Gly   | Asn      | CAa        | Gly  | Asp     | Thr         | Gly      | Thr | Arg   | Ser        | Ala          |
| 145 |           |            |       |           | 150   |          |            |      |         | 155         |          |     |       |            | 160          |
| Gly | Pro       | Leu        | Arg   | Arg       | Asn   | Tyr      | Asn        | Phe  | Ile     | Ala         | Ala      | Val | Val   | Glu        | Lys          |
|     |           |            |       | 165       |       |          |            |      | 170     |             |          |     |       | 175        |              |
| Val | Ala       | Pro        |       | Val       | Val   | His      | Val        |      | Leu     | Trp         | Gly      | Arg | Leu   | Leu        | His          |
|     |           |            | 180   |           |       |          |            | 185  |         |             |          |     | 190   |            |              |
| Gly | Ser       | -          | Leu   | Val       | Pro   | Val      | _          | Ser  | Gly     | Ser         | Gly      |     | Ile   | Val        | Ser          |
|     |           | 195        |       |           |       | _        | 200        |      |         |             |          | 205 |       | _          |              |
| Glu |           | Gly        | Leu   | Ile       | Ile   |          | Asn        | Ala  | His     | Val         | Val      | Arg | Asn   | Gln        | Gln          |
| _   | 210       |            | •     | •         | _     | 215      | _          |      |         | _           | 220      |     | - •   |            | •            |
|     | Ile       | Glu        | Val   | Val       |       | Gln      | Asn        | GIA  | Ala     |             | Tyr      | Glu | Ala   | Val        |              |
| 225 | _         |            | _     | _         | 230   |          | _          | _    |         | 235         |          | _   |       |            | 240          |
| гув | Asp       | IIe        | Asp   |           | Lys   | Leu      | Asp        | Leu  |         | Val         | Ile      | Lys | IIe   |            | ser          |
| •   | -1-       | <b>~</b> 3 | _     | 245       | ••- • | <b>-</b> |            | _    | 250     | _           | <b>-</b> |     | _     | 255        | _            |
| ABN | Ala       | GIU        |       | Pro       | val   | Leu      | wet        |      | GTA     | Arg         | Ser      | ser |       | Leu        | Arg          |
| N 1 | <b>03</b> | 01         | 260   | **- 1     | 1103  | 23-      | <b>T</b> = | 265  | <b></b> | <b>D</b>    | nh -     | 0   | 270   | <b>0</b> 3 | <b>N</b> === |
| WIG | GTÅ       |            | rne   | vaı       | vaı   | ATG      |            | GIĀ  | ser     | PTO         | Phe      |     | ren   | GIN        | ASN          |
| m b | 71-       | 275        | n 1 - | <b>03</b> | T1-   | 1703     | 280        | mb ~ | T       | <b>01</b> - | N        | 285 | 03.00 | T          | <b>01</b>    |
| TUL | WIS       | IUL        | ALA   | GIV       | TTE   | vaı      | ser        | TUL  | TAB     | GTU         | Arg      | CTA | GIA   | TAR        | GLU          |

290 295 300 Leu Gly Met Lys Asp Ser Asp Met Asp Tyr Val Gln Ile Asp Ala Thr 305 310 315 320 Ile Asn Tyr Gly Asn Ser Gly Gly Pro Leu Val Asn Leu Asp Gly Asp 325 330 Val Ile Gly Val Asn Ser Leu Arg Val Thr Asp Gly Ile Ser Phe Ala 350 345 Ile Pro Ser Asp Arg Val Arg Gln Phe Leu Ala Glu Tyr His Glu His 365 360 Gln Met Lys Gly Lys Ala Phe Ser Asn Lys Lys Tyr Leu Gly Leu Gln 375 Met Leu Ser Leu Thr Val Pro Leu Ser Glu Glu Leu Lys Met His Tyr 385 390 395 400 Pro Asp Phe Pro Asp Val Ser Ser Gly Val Tyr Val Cys Lys Val Val 405 Glu Gly Thr Ala Ala Gln Ser Ser Gly Leu Arg Asp His Asp Val Ile 420 425 430 Val Asn Ile Asn Gly Lys Pro Ile Thr Thr Thr Asp Val Val Lys 440 Ala Leu Asp Ser Asp Ser Leu Ser Met Ala Val Leu Arg Gly Lys Asp 460 450 455 Asn Leu Leu Thr Val Ile Pro Glu Thr Ile Asn 465 470 475

#### (2) INFORMATION FOR SEQ ID NO:38:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 266 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

| Met        | Val | Lys | Val | Thr        | Phe        | Asn | Ser | Ala | Leu        | Ala        | Gln | ГÀв | Glu | Ala | Lys        |
|------------|-----|-----|-----|------------|------------|-----|-----|-----|------------|------------|-----|-----|-----|-----|------------|
| 1          |     |     |     | 5          | ·          |     |     |     | 10         |            |     |     |     | 15  |            |
| Lys        | Asp | Glu | Pro | Glu        | Ser        | Gly | Glu | Glu | Ala        | Leu        | Ile | Ile | Pro | Pro | Asp        |
|            |     |     | 20  | •          |            |     |     | 25  |            |            |     |     | 30  |     |            |
| Ala        | Val | Ala | Val | Asp        | Сув        | Lys | Asp | Pro | Asp        | yab        | Val | Val | Pro | Val | Gly        |
|            |     | 35  |     |            |            |     | 40  | •   |            |            |     | 45  |     |     |            |
| Gln        | Arg | Arg | Ala | Trp        | Cys        | Trp | Сув | Met | Сув        | Phe        | Gly | Leu | Ala | Phe | Met        |
|            | 50  |     |     |            |            | 55  |     |     |            |            | 60  |     |     |     |            |
| Leu        | Ala | Gly | Val | Ile        | Leu        | Gly | Gly | Ala | Tyr        | Leu        | Tyr | ГÀв | Tyr | Phe | Ala        |
| 65         |     |     |     |            | 70         |     |     |     |            | 75         |     |     |     |     | 80         |
| Leu        | Gln | Pro | Asp | Asp        | Val        | Tyr | Tyr | Сув | Gly        | Ile        | Lys | Tyr | Ile | Lys | Asp        |
|            |     |     |     | 85         |            |     |     |     | 90         |            |     |     |     | 95  |            |
| Asp        | Val | Ile | Leu | Asn        | Glu        | Pro | Ser | Ala | Asp        | Ala        | Pro | Ala | Ala | Leu | Tyr        |
|            |     |     | 100 |            |            |     |     | 105 |            |            |     |     | 110 |     |            |
| Gln        | Thr | Ile | Glu | Glu        | Asn        | Ile | Lys | Ile | Phe        | Glu        | Glu | Glu | Glu | Val | Glu        |
|            |     | 115 |     |            |            |     | 120 |     |            |            |     | 125 |     |     |            |
| Phe        | Ile | Ser | Val | Pro        | Val        | Pro | Glu | Phe | Ala        | Asp        | Ser | yab | Pro | Ala | Asn        |
|            | 130 |     |     | •          |            | 135 |     |     |            |            | 140 |     |     |     |            |
| Ile        | Val | His | Asp | Phe        | Asn        | Lys | ГÅв | Leu | Thr        | Ala        | Tyr | Leu | Asp | Leu | Asn        |
| 145        |     |     |     |            | 150        |     |     |     |            | 155        |     |     |     |     | 160        |
| Leu        | Asp | Lys | Сув | Tyr        | Val        | Ile | Pro | Leu | Asn        | Thr        | Ser | Ile | Val | Met | Pro        |
|            |     |     |     | 165        |            |     |     |     | 170        |            |     |     |     | 175 |            |
| Pro        | Arg | Asn | Leu | Leu        | Glu        | Leu | Leu | Ile | Asn        | Ile        | Lys | Ala | Gly | Thr | Tyr        |
|            |     |     | 180 |            |            |     |     | 185 |            |            |     |     | 190 |     |            |
| Leu        | Pro | Gln | Ser | Tyr        | Leu        | Ile | His | Glu | His        | Met        | Val | Ile | Thr | Asp | Arg        |
|            |     | 195 |     |            |            |     | 200 |     |            |            |     | 205 |     |     |            |
| Ile        | Glu | Asn | Ile | Asp        | His        | Leu | Gly | Phe | Phe        | Ile        | Tyr | Arg | Leu | Сув | His        |
|            | 210 |     |     |            |            | 215 |     |     |            |            | 220 |     |     |     |            |
| _          | 210 |     |     |            |            |     |     |     |            |            |     |     |     |     |            |
| Asp        | Lys | Glu | Thr | Tyr        | Lys        |     | Gln | Arg | Arg        | Glu        | Thr | Ile | Lys | Gly | Ile        |
| 225        |     | Glu | Thr | Tyr        | Lys<br>230 |     | Gln | Arg | Arg        | Glu<br>235 | Thr | Ile | Lys | Gly | Ile<br>240 |
| 225        |     |     |     |            | 230        | Leu |     |     |            | 235        |     |     |     |     | 240        |
| 225        | Lys |     |     |            | 230        | Leu |     |     |            | 235        |     |     |     |     | 240        |
| 225<br>Gln | Lys | Arg | Glu | Ala<br>245 | 230<br>Ser | Leu | Сув | Phe | Ala<br>250 | 235        |     |     |     | Ģlu | 240        |

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## We Claim:

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1. An isolated and purified human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

- 2. An isolated and purified human protein having an amino acid sequence which is at least 85% identical to an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.
- 3. An isolated and purified human polypeptide comprising at least 6 contiguous amino acids of an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.
- 4. A fusion protein comprising a first protein segment and a second protein segment fused together by means of a peptide bond, wherein the first protein segment consists of at least 6 contiguous amino acids selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.
- 5. A preparation of antibodies which specifically bind to the human protein of claim 1.
- 6. An isolated and purified subgenomic polynucleotide having a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.
- 7. An isolated gene corresponding to a cDNA sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.
- 8. A DNA construct for expressing all or a portion of a human protein having an amino acid sequence selected from the group consisting of the amino acid

sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, comprising:

a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of the human protein, wherein the polynucleotide segment is located downstream from the promoter, wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

A host cell comprising a DNA construct comprising:
 a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID NOs:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the promoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

- 10. A homologously recombinant cell having incorporated therein a new transcription initiation unit, wherein the new transcription initiation unit comprises in 5' to 3' order:
  - (a) an exogenous regulatory sequence;
  - (b) an exogenous exon; and
  - (c) a splice donor site,

wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene.

11. A method of producing a human protein, comprising the steps of:
growing a culture of a cell comprising a DNA construct comprising
(1) a promoter and (2) a polynucleotide segment encoding at least 6 contiguous
amino acids of a human protein having an amino acid sequence selected from the

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group consisting of the amino acid sequences shown in SEQ ID NOs:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the promoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter; and purifying the protein from the culture.

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12. A method of producing a human protein, comprising the steps of:
growing a culture of a homologously recombinant cell having
incorporated therein a new transcription initiation unit, wherein the new
transcription initiation unit comprises in 5' to 3' order:

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- (a) an exogenous regulatory sequence;
- (b) an exogenous exon; and
- (c) a splice donor site,

wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene; and purifying the protein from the culture.

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13. A method of identifying a secreted polypeptide which is modified by rough microsomes, comprising the steps of:

transcribing in vitro a population of cDNA molecules whereby a population of cRNA molecules is formed;

translating a first portion of the population of cRNA molecules in vitro in the absence of rough microsomes whereby a first population of polypeptides is formed;

translating a second portion of the population of cRNA molecules *in vitro* in the presence of rough microsomes whereby a second population of polypeptides is formed;

comparing the first population of polypeptides with the second population of polypeptides; and

detecting polypeptide members of the second population which have been modified by the rough microsomes.

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